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BLOOD GROUPS, SUBGROUPS, M, N TYPES AND Rh SUBTYPES IN FILIPINOS.

By R. T. SIMMONS AND J. J. GRAYDON,
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In recent blood group surveys conducted at these laboratories, it has been found possible to obtain and test blood samples from small but representative series of Australian aborigines, Indonesians, Fijians, Japanese, Papuans and Maoris for blood groups, the subgroups of A, the M, N types and the Rh factor. The results of most of these surveys have been published, while other reports are in the press. This work will be extended to other races in the Pacific when opportunity permits.

This paper presents the results obtained from Filipino blood samples collected on Leyte during December, 1944, at a time when thousands of natives were receiving care and medical attention from the United States Army.

The following extracts concerning the peoples of the Philippines are taken from the "*Encyclopædia Britannica*" (Fourteen Edition):

> The Philippine archipelago first became known to Europeans on March 16th, 1521, through Ferdinand Magellan. But there are authentic Chinese accounts of trading voyages as early as the 10th and 13th centuries, and the contact probably went back much further. A Hindu influence undoubtedly came by way of the Malay peninsula, Java and other islands nearby, and probably reached back to the early centuries of the Christian era. The Hindus influenced the life of the people intimately. Many Sanskrit words in the languages and dialects of the people of the Philippines and the forms of the letters used at the time of their discovery by the Spanish indicate this.
>
> During the interim between Magellan's discovery and the settlement of Manila, the Portuguese actively contested Spanish right to the archipelago. Later came Dutch and others. There are 43 ethnographic groups. The Filipinos proper (the descendants of the Malays christianized by the Spaniards) are composed of 8 peoples. They are the Bisaya; the Tagalog; the Iloko, the Bikol, the Pangasinan; the Pampangan; Ibanag and the Sambal. These are all Christians. The classified pagan peoples are represented by 18 groups, the unclassified pagans by 12 and the Moros by 7. The non-Christians are divided into pygmies, Indonesians and Malays. The first are Negritos (small blacks), who probably represent three quite distinct aboriginal races, viz., the true Negrito; a straight-haired dwarf type of strong mongoloid affinities, to whom the name Proto-Malay has been applied; and the Australoid-Ainu, a dwarf hairy man intermediate between the aboriginal Australian and the Ainu of northern Japan. These three types, however, are now thoroughly mixed. The pygmy types are found in the Apayas swamp regions, the Ilokos mountains, the Luzon mountains, the Bisaya islands and Mindanao. The Indonesions were immigrants who appear to have mixed extensively with the pygmy peoples and others.
>
> The Moros, representing 7 ethnographic groups, live almost exclusively in the Sulu archipelago at the southern end of Palawan, and the Mindanao provinces of Zamboanga, Cotobato and Lanao. Many also live in northern Borneo, and it is not uncommon for them to pass to the Philippines.

The present survey deals with Filipinos of Filipino parents who were born on Leyte and Samar, together with a small sample of individuals born on Luzon and adjacent islands. No Negritoes or pygmy types were included, and the sampling can be regarded as being representative of the "Filipinos proper" mentioned above.

The blood samples were collected by Colonel Howard F. Smith and his colleagues, to whom we extend our gratitude for their interest in this work and their valued cooperation. Colonel Smith, who has a wide knowledge of the Filipinos, having spent many years in the Philippines as a medical officer, selected the subjects from whom the blood samples were collected.

Material and Methods.

The blood samples, which were obtained from 385 Filipinos, consisted of two drops of blood added to one millilitre of the glucose and citrate solution of Rous and Turner (1916), to which had been added "Merthiolate" to give a concentration of 1/100,000. The samples were immediately placed on ice and brought to Melbourne in a "Thermos" flask packed with ice. Through unforeseen circumstances the samples did not reach our laboratory until twenty-four days after collection, but during this period the ice in the flask had been constantly replenished. Only three blood samples in the series showed evidence of hæmolysis and were discarded; the remaining 382 samples appeared to be in perfect condition, and these were all tested within thirty-six hours of arrival at this laboratory. The agglutination results obtained were comparable with those obtained with freshly collected control cells, and no sample was pan-agglutinable.

Throughout all previous blood surveys it has been our practice to ask our collaborators to collect, from a finger thoroughly cleansed with ether, two drops of blood into the rubber-stoppered vials containing one millilitre of the sterile glucose-citrate mixture, to pack the samples in ice in "Thermos" flasks and to return them to us by the first available aeroplane. In most instances the samples have been received at the laboratory within two to five days, and samples from distant parts of Australia, Papua, Fiji and New Zealand have been received in perfect condition. In our own laboratory we have from time to time checked the agglutination reactions of control blood cells stored in glucose-citrate solution at 38° F. Provided the cells were collected with care, there was usually no evidence of hæmolysis, and true agglutination reactions were obtained when tests were made.

Simmons, Graydon and Hamilton (1944) reported that blood samples of different Rh subtypes stored at 5° C. for four months in Rous and Turner's solution containing 0·001% "Merthiolate" showed no evidence of hæmolysis and gave the same result as when first collected. In a recent paper Graydon and Simmons (1945) reported that control blood cells stored at 38° F. in the sterile glucose and citrate solution gave specific group, M, N type and Rh agglutination after storage for eight months. Recently we determined in this laboratory the Rh subtypes of a number of blood samples which had been stored for five months at 38° F., and another set of tests were carried out on freshly collected blood samples from the same subjects by Dr. G. A. Kelsall and Miss D. Nicholas, in Perth, Western Australia. The results obtained in the two series of independent tests were identical (Simmons, Jakobowicz and Kelsall, in the press).

Tests made more recently on blood samples which had been stored at 38° F. for twelve months gave group, M, N and Rh results identical with our previous findings. Bottles of the samples previously unopened were used for the successive tests carried out during the period of twelve months.

It is therefore evident that blood samples collected according to this technique, stored at 38° F. and free from hæmolysis, give specific agglutination reactions for months after collection.

Method of Preparation of Modified Rous and Turner Glucose and Citrate Solution.[1]

The reagents used were as follows: sodium citrate, neutral [2 $(C_3H_4.OH.(COONa)_3).+11H_2O$] (Merck); glucose, pure, reagent quality (several brands have been used and all were found satisfactory).

Two solutions were prepared, 3·8% sodium citrate solution and 5·4% glucose solution in distilled water, and these were autoclaved separately at 110° C. for fifteen minutes. After being cooled, the two solutions were mixed in the proportions used by Rous and Turner, 720 millilitres of the glucose solution to 297 millilitres of the sodium citrate solution, and 1·0 millilitre of a solution of 1% "Merthiolate" was added to give a final concentration of 1/100,000. The mixing was performed in a specially fitted bottle which enabled the mixture to be transferred to sterile two millilitre vials under rigid conditions of sterility. Immediately after one millilitre of the mixture had been added to each vial, it was stoppered with a sterile rubber stopper. The vials were labelled, and numbered on both label and stopper, and brushed with transparent lacquer to prevent loss of labels should the vials become wet in transit. Two drops of blood were added to each vial when the specimens were collected. This slightly modified Rous and Turner solution has now been in use here for six years, and we believe that, by means of this preserving solution, it is possible to obtain blood samples from any part of the world, provided the samples are stored in ice and air transport is available for the return of the specimens to the laboratory.

Results.

The blood grouping results are shown in Table I.

The gene frequencies for 382 Filipinos from Leyte, Samar and nine other islands are as follows: $p = 0·152$, $q = 0·181$ and $r = 0·671$. The frequencies of the three groups tested (see Table I) show some variation within the groups, but are of the same order as those found in previously reported surveys in the Philippines and tabulated by Boyd (1939). The percentage of group B samples found, 27·0 ($q = 0·181$), is the highest we have yet encountered in surveys dealing with Indonesians, Fijians, Japanese and Papuans (Simmons *et alii*, 1945; Graydon and Simmons, in the press). It is also higher than that reported by Boyd for the Indo-Chinese and Formosans. It appears, therefore, that the high percentage of group B must be due, not to admixture with any of the peripheral races as they exist today, but to the earlier Hindu influence which also was found in the language and customs of the people of the Philippines.

Of the 382 subjects tested, 107 were found to belong to blood groups A and AB, and of these, 106 belonged to subgroups A_1 and A_1B. Only one subject was found to belong to subgroup A_2, and this Filipino, a male, aged eighteen years, was born on Samar. The presence of the A_2 factor in this native may have been due to Indian influence rather than to white admixture, as MacFarlane (1943) has reported a low percentage of this factor in Indians of

[1] The red cell suspensions in preserving fluid are tested directly for all group, type and Rh tests. Cells in this fluid give stronger agglutination than that obtained with the washed saline suspensions recommended by other workers.

TABLE I.
Blood Group Frequencies in Filipinos.

Island.	Number of Subjects Tested.	Number and Percentage of Groups.				Frequency of Genes.			D/σ_D
		O.	A.	B.	AB.	p.	q	r	
Leyte	243	108 (44·4%)	53 (21·8%)	65 (26·8%)	17 (7·0%)	0·156	0·186	0·667	0·96
Samar	102	48 (47·1%)	20 (19·6%)	31 (30·4%)	3 (2·9%)	0·120	0·183	0·686	0·90
Luzon and eight other islands	37	16 (43·0%)	11 (30·0%)	7 (19·0%)	3 (8·0%)	0·212	0·146	0·658	0·24
Total	382	172 (45·0%)	84 (22·0%)	103 (27·0%)	23 (6·0%)	0·152	0·181	0·671	0·56

TABLE II.
M, N Frequencies in Filipinos.

Island.	Number of Subjects Tested.	Number and Percentage of Types.			Frequency of Genes.		D/σ_D.
		M	MN	N	*m*	*n*	
Leyte	243	63 (25·9%)	124 (51·0%)	56 (23·0%)	0·514	0·486	0·34
Samar	102	22 (21·6%)	56 (54·9%)	24 (23·5%)	0·490	0·510	1·0
Luzon and eight other islands	37	14 (37·0%)	12 (33·0%)	11 (30·0%)	0·539	0·461	1·9
Total	382	99 (25·9%)	192 (50·3%)	91 (23·8%)	0·510	0·490	0·11

Calcutta. The lack of subgroup A_2 seems to be a regular characteristic of the native races so far tested, as distinct from the white race and the American Negroes.

The results of the M, N tests are shown in Table II.

The *m* and *n* frequencies found ($m = 0{\cdot}510$ and $n = 0{\cdot}490$) show that the Filipino falls into a world-wide group of races with much the same *m*, *n* frequencies. Races so far found to fall outside this group include the Australian aborigines, Papuans, Fijians, American Indians, Eskimos (East and West Greenland), Finns and Bedouins (Syria).

When the blood samples of the Filipinos were received at the laboratory, they were immediately tested for the Rh factor by the slide technique (Simmons *et alii*, 1943), a potent, standard anti-Rh° serum of group AB being used. This serum was used at a dilution of 1/10, although it was known to give complete agglutination on slides at a dilution of 1/30. Of the 382 blood samples tested, 381 (99·7%) were found to be Rh-positive and only one sample was Rh-negative. This sample was then tested with a number of different specimens of anti-Rh serum, but no evidence of agglutination was obtained. The Filipino found to have Rh-negative blood was a male, aged forty-two years, born on Samar of Filipino parents, who were also born on Samar.

In previous blood surveys carried out by us on native races we have been unable to determine the Rh subtypes, because we have not found suitable subtype antisera. The additional antisera required are anti-Rh′ and anti-Rh″, previously known as anti-Rh_1 and anti-Rh_2, which give 70% and 30% reactions respectively with the blood of white persons. The blood samples, after tests for groups, M, N types and the Rh factor had been completed, were stored at 38° F. Some weeks later we obtained small dried samples of subtype serum, anti-Rh′ and anti-Rh″ from England. The dried samples, when dissolved in sterile distilled water, reacted perfectly on slides, and at suitable dilutions were used to test 100 blood samples of group O and A, chosen at random from the available samples of these groups. The blood samples tested showed no evidence of hæmolysis and were not pan-agglutinable. The results of these tests are given in Table III.

In Table III are shown the reactions of the various Rh subtypes with the three testing sera, anti-Rh°, anti-Rh′ and anti-Rh″. The nomenclature used is that recommended by Wiener (1944) and slightly modified by Snyder (1945). The Rh subtype percentages for 100 Filipinos are compared with those obtained from 871 white persons (Wiener, 1944), 138 American Negroes (Wiener *et alii*, 1944) and 150 Japanese (Waller and Levine, 1944).

In the Filipino samples only three Rh subtypes were found—Rh°′ = 87%, Rh°″ = 2% and Rh°′Rh°″ = 11%; these percentages differ considerably from those found for the other three races. In samples from white people the higher subtype percentage is also Rh°′ (53·6), while the American Negroes have an unusually high percentage for Rh° (41·6). In the Japanese the highest percentage found is for sub-type Rh°′Rh°″ (47·25).

Two surveys on Chinese have been reported (Levine and Wong, 1943; Wiener *et alii*, 1944). In both surveys the blood samples were tested with anti-Rh° and anti-Rh′ sera, but not with anti-Rh″ serum, so that the Rh subtypes were not actually determined. Levine and Wong found that the blood of 93% of the Chinese reacted with anti-Rh′ serum, while Wiener found that the blood of 94·9% reacted with anti-Rh′ serum; for comparison it will be noted that the blood of 98·0% of the Filipinos in our series reacted with anti-Rh′ serum. Wiener, in his series, tested with an anti-Rh″ serum seven Chinese blood samples giving negative results with anti-Rh′ serum, and from his tests he was able to state that of 138 Chinese tested, the blood of two was Rh-negative, that of one was Rh° and that of six was Rh°″. Of the remaining 131 samples, the great majority were concluded to be of type Rh°′, while the balance were of type Rh°′Rh°″. From these results it would appear that the distribution of the Rh subtypes in Filipinos as determined by us is probably similar to that in Chinese.

Summary.

1. Blood samples from 382 selected Filipinos, nearly all unrelated adults, mostly born on Leyte and Samar of Filipino parents, have been tested for blood groups, the subgroups of A, the M, N types, and the Rh factor.

2. The group percentages were: group O, 45·0; group A, 22·0; group B, 27·0; group AB, 6·0. Of 107 subjects of blood groups A and AB, the blood of 106 was found to be of subgroups A_1 and A_1B. The blood of one exception, a Filipino born on Samar, belonged to subgroup A_2.

3. The type percentages were: type M, 25·9; type MN, 50·3; type N, 23·8. The *m* and *n* frequencies found indicate

TABLE III.
Rh Subtypes in Filipinos Compared with Whites, Negroes and Japanese.

Results with Rh Antisera.			Result.	Filipinos. (100 Tested.)	American Whites. (871 Tested.)	American Negroes. (138 Tested.)	Japanese. (150 Tested.)
Anti-Rh° (84%)	Anti-Rh′. (70%)	Anti-Rh″. (30%)					
+	+	0	Rh°′	87·0	53·6	21·2	37·4
+	0	+	Rh°″	2·0	13·4	21·9	13·35
+	+	+	Rh°′ Rh°″	11·0	16·8	7·3	47·25
+	0	0	Rh°	0·0	2·5	41·6	0·0
0	+	0	Rh′	0·0	0·8	0·7	0·0
0	0	+	Rh″	0·0	0·5	0·0	0·0
0	+	+	Rh′ Rh″	0·0	0·0	0·0	0·66
0	0	0	Rh-negative	0·0	12·4	7·3	1·34

that the Filipinos fall into a world-wide group of races which possess similar frequencies.

4. Of the 382 samples, 381 (99·7%) were found to be Rh-positive.

5. The tests for groups, types and the Rh factor were made on blood samples twenty-four days old, which had been stored in ice. The samples showed no hæmolysis and none were pan-agglutinable.

6. The Rh subtypes were tested in 100 samples of group A and group O cells selected at random. The samples were forty-five days old when tested; they had been stored at 38° F., and showed no hæmolysis or pan-agglutination. The percentages were: Rh°′, 87·0; Rh°″, 2·0; Rh°′Rh°″, 11·0. These percentages differ from those recorded for white persons, American Negroes and Japanese, but are probably similar to those of Chinese.

7. A method is given for the preparation of a slightly modified Rous and Turner glucose-citrate solution for preserving red cells. Sterile samples of blood stored in this solution at 38° F. for twelve months have been found to be free from hæmolysis and to give specific group, type and Rh agglutination.

Acknowledgements.

We are grateful to Colonel Howard F. Smith and his colleagues, who collected the blood samples for us on Leyte, to Dr. G. L. Taylor, who kindly made available to us dried samples of anti-Rh subtype serum through Dr. G. A. Kelsall, and to Mr. E. F. Woods, B.Sc., and Mrs. Margaret Green, who assisted us during this survey.

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ANTICOAGULANT EFFECT OF PERFUSING ORGANS: LIVER, KIDNEY AND LUNG.

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IT has been shown in a previous communication that when heparinized blood is perfused through the pneumonic lung it acquires increased anticoagulant activity.[4] This was considered due to an output of a substance intimately associated with the vessels. In this paper the work has been extended to the liver and kidney, and an attempt has been made to determine the nature of the anticoagulant. It is believed that this is important *in vivo* in maintaining non-coagulation of the blood, and if so, that it may have a considerable clinical application.

Method.

Heparin Assay.

Heparin (Kahlbaum) was assayed by the method described in a previous paper,[3] toluidin blue (Grübler) being used. Usually the concentration of heparin added was 0·05 milligramme per mil of diluted blood.

Prothrombin Assay.

Rabbit brain was used to estimate the prothrombin time; but, since the plasma was heparinized, Quick's technique[2] was modified. Calcium chloride, 0·02 mil of a 0·02 molar solution, was added to 0·02 mil of plasma, and kept at 37° C. for one minute. Then 0·02 mil of thromboplastin (Quick) was shot into the solution and the stopwatch was started. The clotting time was recorded at 37° C. By reference to the graph (Figure I) the concentration of prothrombin was read directly.

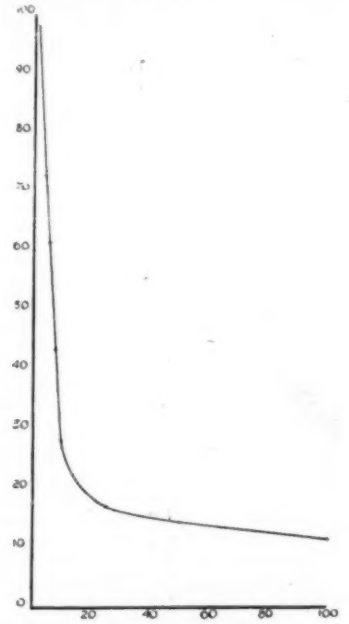

FIGURE I.

Prothrombin estimation. Ordinate: prothrombin time (seconds); abscissa: percentage prothrombin content.

Perfusion Experiments.

Heparinized blood was obtained from the aorta of cats under "Nembutal" anæsthesia and added to nine times its volume of Tyrode as described in a previous communication.[3] The liver was perfused through the portal vein with Tyrode till it was free of blood and then the diluted blood was used for perfusion. The kidney was perfused through the renal artery, similarly, except that the head of pressure was increased to 120 centimetres of water. The fluid obtained from the renal vein and pelvis was collected (sample III). The lung was perfused through the pulmonary artery. The organs were isolated and laid on a glass plate. Samples of perfusion fluid were collected by a syringe from the cannula at the beginning and after one hour's perfusion (samples I and II). The perfused

sample was collected for one hour (sample III). In two experiments, the lung was affected by bronchopneumonia and the extent of the lesion was classified as described previously.[5] The kidneys were normal and the livers appeared normal.

Blood Clotting.

Some of the diluted blood obtained from the samples was left at room temperature, and readings were taken at twenty-four hours. The degree of clotting was assessed as "±" when only a trace of clotting was detected (Figure II), "+" when small clots appeared, and "++" when there was one large clot.

Protein Content of Plasma.

The plasma was diluted to a strength of 1 in 12 with 0·85% saline solution. The solution was boiled with trichloracetic solution and matched against turbidity standards.

Experimental Investigation.

Control Perfusion.

A control was set up in exactly the same way as the experiment, except that no organ was perfused. The blood ran from the cannula onto the glass plate and was then collected. Control samples were taken proximal to the cannula.

Clotting developed in all samples, and there was a slight fall in the heparin content of the plasma of the "perfused" sample. There was no evident change in the prothrombin content of the plasma. These findings are shown in Table I.

TABLE I.
Control Experiment.

Degree of Clotting.			Heparin Content. (Milligrammes per Mil.)			Prothrombin Time. (Seconds.)			Prothrombin Content. (Percentage of Normal.)		
Sample I.	Sample II.	Sample III.	Sample I.	Sample II.	Sample III.	Sample I.	Sample II.	Sample III.	Sample I.	Sample II.	Sample III.
+	+	+	0·057	0·048	0·047	24·3	25·1	22·8	11·5	11·0	12·5

Liver Perfusions.

Heparin Content of Plasma.—Eight livers were perfused. Clotting occurred in control samples of blood (samples I and II) in every instance, while only a trace of clotting, or none, was detected in the perfused blood (sample III). Tests for the heparin content of the plasma were made in the case of five of these livers. There was a slight fall only in the heparin content of the perfusion fluid. For example, in one experiment, the concentration of heparin was 0·050 and 0·047 milligramme per mil in the two samples obtained from the tubing proximal to the liver, and 0·044 milligramme per mil in the perfused sample. A trace of clot only appeared in the perfused sample, while there was considerable clotting in the samples collected proximal to the liver. The findings in the case of Experiment III (Table II) are shown in Figure I, in which the considerable difference in clotting produced in the samples is well shown. It is seen in Table II, where the five experiments are recorded, that there was little change in heparin concentration, while no clotting or very slight clotting was seen in the perfused samples; yet clotting was obvious in the samples taken proximal to the cannula. Evidently this inhibition of clotting cannot be due to an increased concentration of heparin unless the perfused fluid has something additional in it which affects the heparin estimation, a suggestion for which we have no experimental confirmation.

TABLE II.
Liver Perfusions, Heparin Concentrations.

Experiment.	Heparin Concentration. (Milligrammes per Mil.)			Degree of Clotting.		
	Sample I.	Sample II.	Sample III.	Sample I.	Sample II.	Sample III.
II	0·050	0·047	0·044	++	++	±
III	0·050	0·047	0·042	++	++	±
IV	0·048	0·044	0·040	++	+	−
V	0·050	0·047	0·038	++	++	−
VI	0·050	0·048	0·043	++	++	±

Prothrombin Content of Plasma.—Estimations were made of the prothrombin content of the samples described above. In four out of the five there was a slight diminution only in the prothrombin content. In the fourth experiment a considerable decrease was observed. These findings are shown in Table III. It is seen (Table III) that the prothrombin concentration has not fallen sufficiently in the first three and the fifth of these perfusions to account for absence of clotting in the perfused fluid. This is so because, for example, in Experiment IV clotting occurred in the second sample with a prothrombin concentration equal to that of the perfused sample in Experiment II, in which negligible clotting occurred. The concentration of the prothrombin in the perfused sample in Experiment III was greater[6] and still obvious clotting did not occur. In the fourth experiment (Experiment V) the prothrombin concentration in the perfused sample was low enough to account for lack of clotting, but since clotting did not occur with a higher concentration of prothrombin in the other cases, it cannot be that loss of prothrombin accounts for non-clotting of blood perfused through liver. In one liver experiment (Experiment IV) bile was added to a cannula sample, and clotting developed, while in the perfused sample no clot formation occurred. In the perfused samples a faint xanthochromia was observed.

TABLE III.
Liver Perfusions, Prothrombin Times.

Experiment.	Prothrombin Time. (Seconds.)			Prothrombin Concentration as a Percentage of Normal.		
	Sample I.	Sample II.	Sample III.	Sample I.	Sample II.	Sample III.
II	50·0 49·5 50·0	50·3 49·8 50·1	63·4 63·2 62·6	7·5	7·5	6·0
III	37·0 36·2 36·1	37·2 37·1 37·4	43·0 43·4 43·5	9·0	9·0	8·0
IV	53·0 52·0 54·0	60·0 62·0 61·0	68·0 66·5 66·9	7·0	6·0	5·0
V	52·0 52·5 52·4	58·0 57·5 57·0	101·5 101·0 101·5	7·0	6·0	1·5
VI	28·5 29·5 29·4	33·4 33·3 33·5	38·0 38·4 38·3	10·0	9·5	8·5

Kidney Perfusions.

Heparin Content of Plasma.—Four kidneys were perfused and clotting developed in control samples in each instance. No clotting was detected in any of the perfused samples. This differs from the findings in the case of the liver, in which slight clotting was seen not infrequently in the perfused samples. Heparin estimations were made on the plasma obtained from two of the perfusions. In a third (Experiment VIII) the heparin was estimated on the

seventeenth day, when none remained. It has been shown earlier[7] that heparin does not keep in plasma. In the two experiments in which the heparin estimations were made immediately a slight fall was detected in the heparin content; for example, in one experiment perfused fluid contained 0·034 milligramme per mil, while the fluid removed proximal to the cannula contained 0·050 and 0·046 milligramme per mil. Similar findings were obtained in the other experiment (see Table IV). Thus, the absence of clotting cannot be due to increase of heparin in the perfused fluid.

TABLE IV.
Kidney Perfusions, Heparin Concentrations.

Experiment.	Heparin Content. (Milligrammes per Mil.)			Degree of Clotting.		
	Sample I.	Sample II.	Sample III.	Sample I.	Sample II.	Sample III.
VII				++	++	−
VIII				+	+	−
IX	0·050	0·046	0·034	++	+	−
X	0·050	0·045	0·030	++	++	−

Prothrombin Content of Plasma.—In Table V the prothrombin content of the samples is recorded. There was a gross reduction in the prothrombin content of the fluid which had passed through the kidney. One would think that the reduction was sufficient to account for the inhibition of clotting, but the findings in the case of the liver make one hesitant to attribute it entirely to this. However, the fact that in the case of the liver slight clotting was seen in the perfused fluid in some cases, and that this did not occur in the case of the kidney, does suggest that the lowered prothrombin content may account in part for absence of clotting. In addition, in the perfused samples a faint xanthochromia was seen. The addition of concentrated slow-reacting substance,[1] one milligramme per mil, to diluted heparinized blood, did not inhibit coagulation.

TABLE V.
Kidney Perfusions, Prothrombin Times.

Experiment.	Prothrombin Time.			Prothrombin Concentration.		
	Sample I.	Sample II.	Sample III.	Sample I.	Sample II.	Sample III.
VIII	94·0[1]	95·0	134·0	2·0	2·0	?
	94·0					
IX	52·2	56·4	87·0			
	51·3	55·3	86·5	7·0	6·5	2·5
	51·0	56·0	85·8			
X	42·5	47·0	105·0			
	43·0	49·0	106·0	8·0	7·5	1·0
	44·0	49·0	104·0			

[1] Tested on seventeenth day.

Lung Perfusions.

Heparin Content of Plasma.—Four lungs were perfused. A trace of clotting appeared in the perfused fluid in the case of the diseased lungs, but in the case of the normal lungs a trace of clotting appeared in the one sample and small clots in the other. There was again no increase in the heparin content of the perfused fluid. In the case of the slightly diseased lung, there was a slight fall in the heparin concentration, and in the case of the moderately diseased lung very little heparin was found in the perfused sample (Table VI). As described earlier,[7] heparin assay of plasma after some days shows a diminution in the amount of heparin, and this was the case in the second experiment in Table VI, on a healthy lung; but there was no evident difference in the concentration in the samples in this case. Heparin cannot account for the inhibition of clotting in blood perfused through the lung.

Prothrombin Content of Plasma.—In the case of the two diseased lungs on which prothrombin estimations were made, there was an obvious reduction in the prothrombin content of the perfused sample (Table VII). Experiment XIV was performed on the nineteenth day, and this accounts for the low figure of the control; but the control fluid was still markedly greater in prothrombin content than the perfused sample. In the case of the normal lung (Experiment XII) there was no change in the prothrombin content.

TABLE VII.
Lung Perfusions, Prothrombin Times.

Experiment.	Prothrombin Time.			Prothrombin Concentration.		
	Sample I.	Sample II.	Sample III.	Sample I.	Sample II.	Sample III.
XII	58·0	62·0	63·0			
	55·0	63·0	64·0	6·0	5·5	5·5
	59·0					
XIII	65·0	66·0	93·0			
	66·0	66·0	95·0	5·0	5·0	2·0
	65·0	66·0	93·5			
XIV	97·0[1]	93·5	135·0	1·5	2·0	?

[1] Tested nineteenth day.

Platelet Content of Samples.

In five cases platelet counts were performed on the blood samples. The findings are shown in Table VIII.

TABLE VIII.
Platelet Content of Blood (Diluted).
Number of Platelets per Cubic Millimetre.

Organ.	Experiment.	Sample I.	Sample II.	Sample III.
Liver	III	18,000	21,000	12,000
Liver	IV	50,000	41,000	28,000
Kidney	VIII	51,000	29,000	20,000
Lung	XII	27,000	21,000	18,000
Lung	XIV	69,000	77,000	67,000

Though there is a fall in the platelet count of the perfused sample, it does not seem that this can account for the lack of clotting, because the lack of clotting is not graded with the platelet count. For example, in Experiment VIII clotting occurred in an unperfused sample with a lower platelet count than that of the perfused sample of Experiment XIV, in which no clotting occurred. Also it is well known that platelets are not essential for clotting. This has been discussed in an earlier paper.[6]

TABLE VI.
Lung Perfusions, Heparin Concentrations.

Experiment.	Extent of Lung Lesion.	Amount of Heparin by Weight. (Gramme.)	Heparin. (Milligrammes per Mil.)			Degree of Clotting.		
			Sample I.	Sample II.	Sample III.	Sample I.	Sample II.	Sample III.
XI	Normal lung.	0·02				+	+	±
XII	Normal lung.	0·05	0·014[1]	0·016	0·016	+	+	±
XIII	Slightly diseased.	0·05	0·050	0·048	0·047	+	++	±
XIV	Moderately diseased.	0·032	0·032	0·036	0·006	++	++	±

[1] Plasma tested after three days.

Protein Content of Samples.

Estimations were made on the protein content of the samples. There was a slight fall in the protein concentration of the perfused fluid as compared with the samples obtained from the cannula (Table IX); for example, the pooled figure in the nine cases in which this estimation was made was 322 milligrammes *per centum*, compared to 331 milligrammes *per centum* for the cannula samples.

TABLE IX.
Protein Content of Plasma.
(Milligrammes per 100 Mils.)

Organ.	Experiment.	Sample I.	Sample II.	Sample III.
Liver	II	340	360	320
Liver	III	320	340	360
Liver	IV	300	320	300
Liver	V	288	300	264
Kidney	VIII	350	385	315
Kidney	IX	360	380	340
Kidney	X	300	310	325
Lung	XII	290	335	325
Lung	XIII	340	340	360
Average..	.. ..	321	341	322

Fibrinogen Content of Plasma.

The fibrinogen content of control samples from a liver perfusion experiment were compared with the perfused sample in which no clotting had occurred; the respective contents were 0·032 gramme *per centum* for each of the cannula samples and 0·020 gramme *per centum* for the perfused sample. In this experiment the difference in the fibrinogen concentration equalled the difference in the protein concentration of the two samples. There is insufficient reduction in the fibrinogen content to account for the difference in clotting of the two samples.

Calcium Content of Plasma.

The calcium content was estimated in two liver experiments, in which a considerable difference in clotting was observed. There was little change in the calcium content of the plasma; there was 6·4 milligrammes *per centum* in the plasma passing to the organ and 6·7 milligrammes *per centum* in the perfused fluid in one experiment (III). In the other experiment (IV) values of 6·6 milligrammes *per centum* for the plasma before perfusion and 7·0 milligrammes *per centum* for the perfused fluid were obtained.

Prothrombin Concentration of Plasma.

The prothrombin concentration of plasma was determined by reference to a standard plasma which had a clotting time of 11·5 seconds. Dilutions of 50%, 25%, 10%, 8%, 6%, 4% and 1·5% in saline solution were tested. The times were 14·3; (duplicates) 17, 17·2; 28, 28; 43, 44; 62, 61; 73·5, 74; and 96, 100 seconds. These findings are shown in Figure II. By reference to the graph prothrombin times were recorded in terms of percentage prothrombin (standard = 100).

Effect of Heparin on Prothrombin Time.

The concentration of heparin has an effect on the prothrombin time—the higher the concentration of heparin, the slower the prothrombin time; for example, in one experiment plasma was divided into lots containing 0·03 and 0·06 milligramme of heparin per mil. The prothrombin time for the first was 29 seconds (28, 30, 29) and for the other 42 seconds (43, 42, 41).

Nature of Anticoagulant Substance.

It is possible that the anticoagulant acting here is that described by de Sütö-Nagy.[4] He points out that there are two fractions obtainable from tissues, one that will accelerate coagulation, associated with globulin, and the other associated with the albumin which delays coagulation. Since, in the case of the liver, no evidence was obtained from the investigation of the well-recognized clotting substances to explain the phenomenon, liver samples were used for extraction. The centrifuged plasma from Experiments II, III, IV and V was divided into two lots (nineteen mils), one containing control unperfused fluid and the other perfused fluid. The plasma was extracted four times with ether for fifteen minutes in a shaker and left to stand for fifteen minutes. The ether fractions were mixed and the mother liquors set aside. The ether fractions were boiled to dryness over a hot water bath, and dried *in vacuo*. The material so obtained was taken up in Tyrode and mixed with diluted heparinized blood (1/10) to two mils. Clotting occurred with control and perfused samples. Then the mother liquors were distilled *in vacuo* to dryness at 30° C. They were then shaken up four times with boiling ethanol (100%) which was poured off each time. The remaining plasma residue was further similarly extracted by being shaken up three times with boiling chloroform and ethanol (3:1). The residue remaining after this procedure was taken up in four mils of Tyrode, and the perfused reconstituted solution was slightly xanthochromic. To each solution, four mils of diluted heparinized blood were added to make a 1 in 10 dilution of blood. The unperfused control sample clotted in four hours, while in the perfused sample no clotting had occurred in four hours and only a trace in twenty-four hours. A control sample of the heparinized blood diluted in Tyrode (1/10) similarly clotted. Thus the activity must be due to an anticoagulant and not lack of a coagulant like thromboplastin.

In another experiment forty mils of plasma were used and treated similarly. In the final residues taken up in tyrode, faint xanthochromia was seen in the perfused sample, but not in the unperfused sample. In the unperfused sample, when added to diluted blood, considerable clotting occurred in twenty-four hours, and in the perfused sample no clotting occurred.

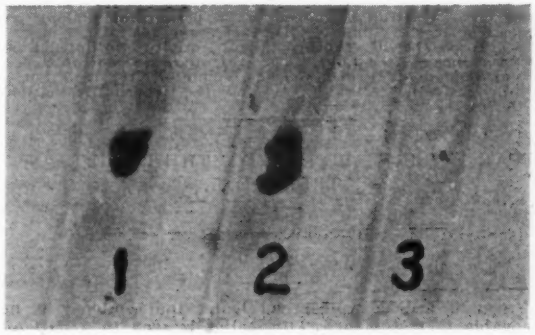

FIGURE II.
Appearance of clot from equal samples of blood before (1 and 2) and after (3) perfusion of the liver. The calcium, heparin and prothrombin content was little altered in these specimens. Readings at twenty-four hours.

Discussion.

It has been shown[4] that tissue extract contains an anticoagulant substance in the albumin portion (lipid-protein). It is also known that heparin will inhibit coagulation, and this is found in muscle, lung and liver.[3] The fact that the perfusion of organs endows the perfused fluid with the property of preventing coagulation may suggest that there is an output of albumin fraction or of heparin. The work of this paper shows that the prothrombin content of blood is reduced by perfusion through the kidney and lung, and this may be a factor operating here. The fact that perfusion of the liver confers a similar property on the perfused fluid while the prothrombin content is unaffected clearly shows that lowered prothrombin content cannot account for this phenomenon. Similarly, heparin does not appear in increased amounts in the perfused fluid, nor is there in other clotting factors, such as fibrinogen *et cetera*, a sufficient change to be responsible. Bile is not active in this regard, nor is slow-reacting substance, which has a colour similar to the active solution. Further, after extraction of the perfused fluid with lipin-solvent, the

mother liquor is still highly anticoagulant. This does not preclude the likelihood that a lipin attached to a protein is responsible.

It appears that this property, whatever substance is responsible, is an important one in maintaining the fluidity of the blood.

Summary.

Heparinized blood perfusion of the liver, kidney and lung endows the perfused blood with considerable anticoagulant activity.

This effect in the case of the liver cannot be ascribed to changes in the heparin, calcium, prothrombin, fibrinogen or platelet content.

In the case of the kidney there is a considerable reduction in the prothrombin content which may contribute to the effect.

In the diseased lung a fall in the prothrombin content may contribute to the effect.

The active solution is faintly xanthochromic and the mother liquor is highly anticoagulant after extraction with lipin solvent.

Acknowledgements.

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CAN EPILEPSY BE CURED? THE RESULTS OF TREATMENT.

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THERE is still a widespread belief that epilepsy is not amenable to treatment. This belief is seen in a patient's reaction to the question: "What is the matter with me?" If he suspects the answer is epilepsy, he becomes distressed because he believes it a hopeless condition—a condition for which there is no satisfactory treatment. It is with an air of despondency that he goes on to ask pitifully: "Can I be cured?" Such an attitude partly derives from the not uncommon medical practice of confining treatment to the exhibition of a standard dose of sedative. If this measure fails, as it frequently must, the person is told that nothing more can be done for him.

It is the purpose of this communication to question this attitude, to show by an analysis of clinical material that the outlook in epilepsy is not so gloomy. Before this is done it is desirable to consider certain aspects of epilepsy in order to appreciate better what we can expect from treatment. These aspects lie in the answer to several questions: What is the nature of epilepsy? Is there any need for treatment? What is the treatment available? After these questions have been answered it will be pertinent to revert to the original proposition: "Can epilepsy be cured?"

What are we Treating? The Nature of Epilepsy.

In the treatment of any complaint a clear understanding of its nature and its mode of progress is a cardinal necessity if we are going to assess the worth of our attempts to modify the natural course of the disease. Although this principle is easily enunciated, its application in practice is not always implemented, for many obvious reasons. There is our ignorance of causation, especially of constitutional factors. There is the constantly changing picture of disease processes—Nature is not static. There is the variation from person to person of the symptom pattern, if we are not content to be mindful only of outstanding features. And equally important, there are the factors emanating from the nature of man's intellect.

Since Grecian times, when man became aware of his powers of abstract thought, he has been enraptured with the visions and theories of his own making. He seldom seeks their confirmation in reality. So he develops fanciful theories on ways of life—democracy, communism, fascism and the like. They have led to war, and will continue to do so because of their remoteness from the actual nature of man. Similar ideation has permeated medical practice. The existence of many fanciful theories on ætiology is an obvious example. Another concerns nomenclature; here we can flaunt our intellect in creating high-sounding terms for certain symptoms and then become smugly satisfied to regard them as entities needing no further study. This applies to epilepsy. It would seem an entity, a well-defined entity. Yet if we return to reality, to clinical observations, and examine this pattern closely in the naturally occurring or in the artificially induced seizure, variations will be found in the same person and from person to person. This entity of epilepsy becomes even less clear cut if the other less dramatic phenomena of epilepsy are brought into consideration. There is a need, then, for a constant examination of our words and ideas, to ensure that they are in harmony with and apply to the actual processes of Nature, and do not merely become the conceptions and opinions derived from non-factual thinking.

These few statements show some of the pitfalls in the understanding of disease processes, even if undistorted by ways and means devised by man to better the workings of Nature. They can now be illustrated by the disorder described as epilepsy. So I should first like to stress the fact that epilepsy is merely a name, the name for a group of symptoms. Like any other symptom-complex, it can vary in its severity, in its duration, in its frequency and in its causation. It may vary in severity from the major seizure, through lesser turns with loss of consciousness and automatism or falling, to conscious states of headache or irritability. There is a similar variation, too, in the duration of the symptoms. Usually the symptoms are momentary, but in some instances they may persist for days or weeks. Such prolonged manifestations are commonly overlooked. The frequency of epileptic reactions also shows wide variations; it may vary from the occurrence of many seizures a day to a single seizure in the patient's lifetime. The failure to appreciate this time factor has led to the supposition that convulsions of childhood are different entity from the malady of adults.

Perhaps the clearest understanding of the symptomatic nature of epilepsy emerges from an examination of its causation. In orthodox descriptions epilepsy is described as either idiopathic, in which there is no cause for the seizures, or secondary, in which the seizures are the outcome of some physical disease, as a cerebral tumour or uræmia. But if we closely examine these groups we shall find that the groupings are not so clear cut. There are rather four groups, merging one with another. In the majority of persons, 90% to 95% of the population, an overwhelming stress, an electrical shock or "Cardiazol", will evoke seizures. In the next group, 5% to 10% of the population, only a severe physical disorder, a tumour or a severe infection, will evoke seizures. This group includes those affected by the secondary or symptomatic epilepsies. The constitutional predisposition partly explains why not all such disorders are associated with seizures. The third group of persons experience epileptic phenomena upon slight stress, such as worry, colds or menstruation. The symptoms of a large portion of the so-called idiopathic epileptics are precipitated by such causes. In the last group there is no obvious cause for the seizures, although careful examination will reveal either lesser degrees of the factors just enumerated or intrinsic abnormal neural fun-

tioning in the cerebral structure. In causation the proportion of stress to constitutional predisposition is variable. These considerations can be graphically illustrated (Figure I).

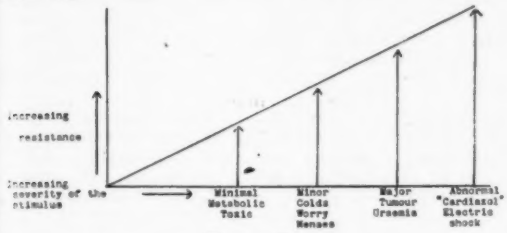

FIGURE I.

These statements should serve to emphasize the fact that epilepsy is merely a symptom-complex, the outcome of the time-honoured soil-seed relationship. The many variations of this relationship underlie the wide range and diversity of the clinical picture of epilepsy; they emphasize that if the disposition is present, the tendency to epileptic disorder is lifelong, though the irritability of nervous tissues lessens with age. These considerations also emphasize the extreme variability of the course of the disorder in each person. This creates great difficulties in assessing the worth of any type of therapy. A few practical examples will illustrate these suppositions. Should a person be having seizures every day, the effect of treatment will soon be obvious; but when the seizures occur at intervals of one or two years the worth of treatment will take years to establish. Again, when seizures are aggravated by emotional upset or fever one cannot foretell the likelihood of such occurrences.

A boy, aged eighteen years, had weekly seizures, which had been controlled for twelve months. He felt very well, so he took on a strenuous job, worked overtime and neglected his meals. He lost weight, but remained free of seizures. Nine months later he cut his arm, and this started a severe cellulitis. Sulphanilamide was given, and within two days he had a seizure.

In this case one sees the constitutional tendency aggravated by fatigue and malnutrition. On this background either the toxic factors from the infection or the potent drug acts as the immediate exciting agent of his seizure. At the same time this boy has learnt a lesson, and an increase in sedative should make his future more secure; but one cannot be certain that excessive domestic worries or other unfortunate circumstances may not arise and initiate further symptoms. Although treatment has had a considerable beneficial effect, yet one cannot regard his complaint as cured.

These are but some of the problems in evaluating the results of therapy. The wide variation in the course of the disease will obviously prevent a mathematical exactitude in assessing the results of treatment.

Is there any Need for Treatment?

Is there any need for treatment? This may seem a rather facetious question. It is less so if we realistically examine the symptoms of epilepsy, seeking especially the harmful aspects. For this purpose it is most practical to consider the symptoms in two groups—the symptoms of which the patient is unconscious (especially the major seizure) and, secondly, the symptoms of which the patient is aware (irritability, headache, depression and so forth).

It is usual to believe that there is great danger to life or limb from a major seizure. For this reason patients are restricted to a limited, uninteresting existence. They worry over their inactivity—a mental state causing more symptoms. Although there is some danger, I do not believe it is great. It is probably no greater than the risk we all run of a street accident. Too often the injuries of these persons are the result of associated abnormalities, mental defectiveness and inadequate manual dexterity. So, although physical danger would theoretically be a frequent and potential accompaniment of seizures, it is in reality not an essential outcome of them. It in itself is not a major indication for treatment. A second consideration lies in whether the seizures produce cerebral damage, aptly put by the question: "Will the turns affect my mind?" This risk again is likely only if the seizures are frequent and occur in that small group of persons whose epilepsy is the manifestation of a brain predestined to early degeneration and readily affected by any stress. I believe that in most persons the effect of the seizures is only temporary. The fear of the seizures, the fear of doing unpleasant and asocial acts at such times, and the fear of their leading to unemployment, are vital worries to many sufferers. These fears are also the major concern of relatives, especially parents whose only child suffers. They are also the fears of the employers and of the community at large. There is perhaps a greater indication for treatment in the management of these fears and anxieties than in the prevention of injury.

The second group of phenomena includes sensations of which the patient is aware. These are headache, periods of irritability, depression, the various auras *et cetera*. Such symptoms are most upsetting and incapacitating, if prolonged or frequent in their occurrence. They require treatment.

From this brief discussion it is apparent that the physical dangers of epilepsy are not so urgent an indication for treatment as are the psychological aspects and the upset occasioned in the person's work programme and daily activities. Treatment, too, is needed for the sake of relatives and the community, who hold a traditional belief in the danger and seriousness of this malady. So if we assume that it is reasonable to avoid the development or lessen the severity of these symptoms, it is now opportune to consider briefly the measures by which this can be achieved.

The Treatment of Epilepsy.

The treatment of epilepsy is the treatment of any symptom. It is based on a carefully taken clinical history to permit an assessment of the nature, the severity, the frequency of the disorder and the factors contributing to its production. There is also the need for a general and neurological examination to exclude any physical basis. A general scrutiny should be made of the patient's way of life, to insure that he has work in keeping with his ability, that he has suitable recreational activities, that he is free from worry and emotional conflict, and that he has an adequate diet, sufficient rest and other requisites providing the basis of good health. He is encouraged to lead a sensible life without restrictions. He and his relatives are given a formulation of the disorder in keeping with their understanding. These are methods aimed at removing and lessening any stimuli that may initiate epileptic symptoms.

It is after these measures have been implemented that the aid of drugs is sought. Their aim is to raise the constitutional resistance so that epileptogenic stimuli lose their potency. To this end any drug that alters cerebral functioning will have some use, but for the majority of persons certain drugs are most effective. These are diphenyl hydantoinate, the barbiturates, bromide, chloral hydrate and, in isolated instances, benzedrine and endocrine and other products. One must also emphasize that the required drug varies from person to person, as does the dosage. Half a grain of phenobarbitone may be adequate for one subject, whilst another requires eight grains. So, too, a combination of drugs is often more efficient than one alone. It is only by trying out these varying combinations that the maximum relief will be given to each patient.

It is my custom to commence treatment with a capsule of "Dilantin" (1·5 grains) three times a day and phenobarbitone (one grain at night). If this fails, the dose of phenobarbitone is increased. Then each of these drugs is increased to tolerance or either alone is exhibited. If this line of therapy fails, the other barbiturates, bromides or chloral hydrate are given. In the majority of cases a combination of "Dilantin" and phenobarbitone has been used, and I think is more successful than either drug alone.

Under this routine treatment toxic symptoms have been uncommon. It has perhaps tended to excessive dosage; but I believe it desirable to raise the threshold above the mini-

mum, to provide a margin of reserve for any excessive stresses that may arise. This routine method also shows that it takes considerable time to try the effect of the different measures in refractory cases, so that the assessment of results cannot be made quickly.

These few remarks on treatment are offered rather to emphasize the principles of treatment than the detailed practical management of this symptom-complex. I shall now examine the results attained by treatment given on these lines.

The Results of Treatment.

The basic purpose of this paper is an attempt to answer the question: "Can epilepsy be cured?" This is the patient's first concern after he has been told the nature of his malady. He desires to know what can be done for him and whether he can be cured.

With regard to the latter question, it is obvious that the condition cannot be cured, as it lies in his constitution. He can be told only that his seizures can be controlled, that they are the outcome of a nerve deficiency, and that if he leads a well-adjusted life and takes the requisite drugs regularly his health should be relatively normal.

The published reports on the treatment of epilepsy are disappointing, in that they do not cover large series of cases, nor do they embrace the treatment over a period of time. Most reports are concerned with the anticonvulsant value of the different drugs. They record how the seizure frequency is altered over a specified period of time by different measures. This method has value, but it neglects the study of the subject in general. It fails to emphasize how far treatment restores the patient, as a unit, to the social structure. This method also minimizes the unpredictable stresses that arise to alter the course of the disease in each person. It presumes that the seizure frequency follows a regular pattern—an hypothesis perhaps applicable only to inmates of institutions.

The worth of any treatment should rather be estimated in the light of its purpose. This purpose of treatment is surely to remove or ameliorate the causes of symptoms, so that the patient is reestablished in harmony with his environment. This applies to epilepsy. An attempt should be made to assess the person's disability and how it has been lessened by treatment. This would entail an estimation of his fears, his employability, his mood upset and the like. Most of these qualities are not readily tabulated, so I have used the seizure frequency as a measure of them. In practice it is a reasonable yardstick if graduated by the degree of disability rather than by the frequency of seizures. On this basis I have classified the response to treatment by the following groupings.

Types of Response to Treatment.

Condition Controlled.—In the first group are included persons who I believe will be free of symptoms provided they continue with treatment. In the face of exceptional stress symptoms may arise. The average period for which this group has been under treatment is three years. If a person is free of seizures for this time, it is usually suggested that treatment can be stopped. My personal opinion is strongly against this advice because of the constitutional nature of the malady. With advancing age the dosage can be lessened, but the habit of taking some medicine regularly is little inconvenience for the freedom from anxiety of further turns.

Condition Probably Controlled.—In the second group are included persons who have been symptom-free for a period of twelve to eighteen months. I believe the majority will remain so and eventually be classified with the controlled group.

An Occasional Aura.—The persons of the third group experience an occasional warning of a seizure without its eventuation. They are conscious of any symptoms they experience. This means that their dosage of sedation is not quite adequate, or that they have had an excessive worry or suffered an acute sickness. For practical purposes this group can be regarded as "relieved", as their actual disability is minimal.

One or Two Seizures a Year.—The frequency of the seizures in the fourth group has been reduced to a maximum of one or two a year. In many instances such occasional seizures have not caused disability, especially when they occur at night or some other time of relaxation. Again, with further treatment, it is likely that these infrequent turns will be abolished in many cases. I have not classified here those persons whose seizures occur at infrequent intervals.

Condition Much Improved.—I have included in the fifth group patients whose seizures have diminished in number and intensity. For the whole group the seizures were one-eighth as frequent as before treatment. The minimum improvement used as a criterion for inclusion in this group was a diminution of the seizures by one-quarter. As well as lessened frequency of the seizures, the latter often become milder in nature. Often, too, the person's sense of well-being was improved, especially in that he became less irritable.

Slight or No Improvement.—In some of the sixth group the turns were one-half or one-third as frequent as before treatment. Others, erratic with treatment, or the assessment of whose condition is difficult, are also included. It can be stated that if treatment is persisted with, there are few cases in which some improvement will not be obtained.

Comment.

I have regarded these groupings as practical. They indicate what the patient can expect from treatment. I have used them in my endeavour to assess the results of treatment. For this purpose I have examined the records of 500 patients examined in private and hospital practice. Of this number, 266 have been under treatment for a sufficient length of time to allow reasonable assumptions to be made. Some criticism of the selection of the patients may be valid, in that a certain percentage, so far refractory to treatment, have been omitted because the length of treatment has been judged inadequate. I have been mindful of this tendency, as well as of the pitfalls already discussed, in tempering judgement concerning a successful result. I have felt that an intimate knowledge of the persons concerned would minimize such difficulties. The general results are set out in Table I.

The patients have been listed according to their sex and to whether they received private or hospital treatment. This table is presented to indicate the general results of treatment. It shows that the condition of 20% of patients is controlled, that the condition of 27% is likely to be controlled, that 4% have an occasional aura, that 14% have one or two seizures a year, that the condition of 24% has been substantially improved, and that 11% have derived little benefit. These groupings could be further condensed and the results expressed in a more practical fashion as follows: the condition of 50% (first, second and third groups) is controlled; 40% (fourth and fifth groups) are reasonably benefited; 10% (the sixth group) make no great progress.

Considering the varied nature of the malady and its frequent severe forms, I think these results are satisfactory. I think they compare favourably with the treatment of any other chronic malady. After a further period of observation it is likely that a number here classified in the lower groups will enter the "controlled" groups, whilst others, impatient or dissatisfied with treatment, will be relegated to the sixth group.

It is now pertinent to ask what are the factors leading to the variable results in treatment? Why cannot the condition of everyone be controlled? Although the number of cases used should be adequate, yet it is not so, because of the extreme variability of the disorder. Yet a detailed study of this material does give some confirmation of generalizations that one would expect from a theoretical consideration of the malady.

Factors Affecting the Results of Treatment.

Sex.—In Table II the results with regard to sex distribution have been tabulated on a percentage basis. This suggests that sex differences have little significance in the overall results of treatment.

TABLE I.

Type of Patient.	Condition Controlled.	Condition Probably Controlled.	Occasional Aura.	One or Two Seizures a Year.	Condition Improved.	No Improvement.	Total.
Private (male)	13	22	2	4	8	4	53
Hospital (male)	13	24	4	21	15	15	87
Private (female)	14	9	—	1	15	2	41
Hospital (female)	13	17	5	12	26	12	85
Total	53 (20%)	72 (27%)	11 (4%)	38 (14%)	64 (24%)	28 (11%)	266

TABLE II.

Sex of Patient.	Condition Controlled.	Condition Probably Controlled.	Occasional Aura.	One or Two Seizures a Year.	Condition Improved.	No Improvement.
Male	18%	33%	4%	18%	17%	10%
Female	22%	21%	4%	10%	33%	11%

TABLE III.

Type of Treatment.	Condition Controlled.	Condition Probably Controlled.	Occasional Aura.	One or Two Seizures a Year.	Condition Improved.	No Improvement.
Private	29%	33%	2%	5%	25%	6%
Hospital	15%	24%	5%	19%	24%	13%

Type of Treatment.—In Table III groupings are made according to whether patients receive private or hospital treatment. The latter patients have to report each month, whilst this frequent interviewing, even were it desirable, is not so feasible in private practice. Among the patients attending hospital there is a greater percentage of severe epilepsy. There is not a great difference in the outcome of treatment, as the principles employed are identical in both places.

Frequency of Seizures.—Frequent seizures provide an advantage, in that their occurrence allows a more ready measure of the success of therapy than when seizures occur infrequently. In the main, the frequency of seizures is an indication of the severity of the disorder, and so when frequent seizures occur treatment should be less effective. Despite this generalization, many persons with very frequent seizures do remarkably well. The reasons for this will be apparent only when a larger series of such persons has been examined, with careful attention to the pattern of the disorder in each individual.

Personality Type.—Personality type again is very important. It not only determines the patient's ability to cooperate and his persistence with treatment, but it also reflects his neurological structure. Gross abnormalities in this, especially as reflected in intellectual defectiveness, predispose the patient to seizures and make him less amenable to treatment. In Table IV the ratio of the persons with normal and high to low intelligence in the different groupings is given.

TABLE IV.

Group.	Normal and High Intelligence.	Low Intelligence.
Condition controlled	6·0	1·0
Condition probably controlled and occasional aura	3·4	1·0
One or two seizures a year	1·3	1·0
Condition improved	1·8	1·0
No improvement	0·6	1·0

Table IV shows that patients with poor personalities do less well than those of normal intelligence, but again there are many striking exceptions. The answer lies in the different neurological structures that underlie clinically apparently similar personalities.

Type of Seizures.—It is usual to suggest that *petit mal* responds less well to treatment than *grand mal*. I am sure that this statement is fallacious. It presumes that all types of *petit mal* are similar. It ignores the principle that the same function may be served by many types of structure. I have found that certain types of *petit mal*, which are only lesser manifestations of the major seizures, respond well to treatment. Just as certain types of major seizures are refractive to treatment, so too are any other of the clinical types. Again, I have not an adequate series to make detailed pronouncements on this feature.

Type of Treatment.—The type of treatment, as has already been stressed, is an individual matter. The majority of my patients are taking a combination of "Dilantin" and phenobarbitone, usually three capsules of "Dilantin" and one or two grains of phenobarbitone a day. When this measure fails, stabilization tends to be difficult and prolonged.

Conclusions.

These figures have been reported in order to give some definite information to patients with epilepsy when they ask: "Can I be cured?"

I believe that the results of treatment are more satisfactory than is customarily believed. Such treatment will be effective only if it is based on a clear evaluation of the disorder in each case. When this is done, it is reasonable to expect that 50% of patients will have their seizures controlled, 40% will be much relieved, and 10% will not make obvious improvement.

A NOTE ON THE INCUBATION PERIOD OF SCRUB TYPHUS AND ITS CORRELATION WITH CLINICAL SEVERITY.

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AN outbreak of scrub typhus in northern Queensland, following a brigade exercise early in 1944, gave an unusual chance of ascertaining the incubation period. The brigade

landed on the coast and bivouacked for the night. The next day the troops moved about a quarter of a mile inland and again bivouacked. The following day the brigade moved off by road to areas from which no scrub typhus has been reported. The day or night on which all the infections were contracted was determined by the Assistant Director of Medical Services of the division, Colonel H. M. Fisher, to whom I am indebted for the information. He found that some of the men infected were ashore only on the second day and night, whereas no man ashore for the first day and night only contracted the disease. It is reasonable to suppose that all infections occurred at the second bivouac.

The incubation period is the number of days from the day or night of infection until the first symptom appears. The day following the day or night of infection is counted as the first day. If it be assumed, then, that all the infections were contracted on the same day, Table I shows the incubation period for 21 cases.

TABLE I.

Days from Exposure.	Number of Cases.
12	12
13	3
14	—
15	2
16	1
17	2
18	1

About 55 subjects who contracted scrub typhus at the same time were treated elsewhere. Only one death occurred in the whole outbreak.

Table II shows the relation between the length of the incubation period and the clinical severity of the disease.

TABLE II.

Clinical Severity.	Incubation Period in Days.							
	12	13	14	15	16	17	18	Totals.
Fatal ..	1	—	—	—	—	—	—	1
Very severe	2	—	—	—	—	—	—	2
Severe ..	7	—	—	—	—	—	—	7
Moderate ..	1	1	—	—	—	1	—	3
Mild	1	1	—	1	—	1	—	4
Very mild ..	—	1	—	1	1	—	—	3
Subclinical ..	—	—	—	—	—	—	1	1
Totals ..	12	3	—	2	1	2	1	21

While these numbers are too small to have much significance, there seems to be some correlation, as in all the most severe cases the shortest incubation period (twelve days) was observed, while infections following the longer incubation periods were all moderate, mild or subclinical.

The range in Proteus OXK titres for these 21 cases was as follows: "negative" (less than 1/80), 2 cases; "partial positive" (1/80), two cases; "positive" (over 1/80), 17 cases.

Two patients were not admitted to hospital. These infections were discovered by the performance of Weil-Felix agglutination tests on 50 men from two of the battalions which had been exposed on the exercise. Twenty-five were picked from men who admitted to some malaise or minor illness within the limits of the known incubation period. They were clinically examined on the twenty-ninth day from exposure and agglutination tests were performed. Two infections were found; brief details are shown in Table III. Both men had been attended by the regimental medical officer. Scrub typhus was not suspected, and neither man had been ill enough to be sent to hospital.

The other group of 25 men from the same units, examined thirty-five days after exposure, had suffered from no illness

TABLE III.

Name.	Days After Exposure Examined.	Incubation Period.	Symptoms.	Period of Illness.	Proteus OXK Titre.
Pte. As.	29	13	Chilly feeling, headache and myalgia.	12 days.	1/6,000
L/Cpl. Na.	28	18	Headache and coryza.	3 days.	1/1,600

of any kind in the incubation period. All their sera gave negative results to the Weil-Felix tests, the titre range for Proteus OXK being nil to 1/60. Thus it seems probable that subclinical or inapparent infections were uncommon.

As a general rule, in laboratory animals the larger the dose of infecting organisms, the shorter is the incubation period and the more severe is the resulting infection. There is usually, in experimental infections, a minimum incubation period which cannot be shortened, however large a dose is given. The minimum incubation period in this outbreak was twelve days, which figure agrees with the general experience of scrub typhus in the Australian Military Forces.

Since all these patients were infected in a small area, it is probable that a single strain of Rickettsia was responsible for the infections, and it seems a reasonable hypothesis that variations in the doses of rickettsia received from infected mites were responsible for the correlated variations in the severity of the disease and the incubation period.

Acknowledgement.

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A METHOD OF CONTINUOUS INTRAMUSCULAR INFUSION OF PENICILLIN SOLUTIONS.

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(From an Australian Military Hospital.)

THE administration of penicillin by a system of continuous infusion has been recently advocated by means of both the intramuscular and intravenous routes. The Edinburgh University apparatus[1] ("Eudrip") is designed to deliver intramuscularly a small quantity of fluid *per diem* with a complicated control of the air intake for accurate regulation. Herrell,[2] in America, reported a series of cases in which continuous intravenous infusion was given with an apparatus of the type now standardized for intravenous therapy.

The purpose of this investigation has been to determine the efficiency of a standard army transfusion set, modified to provide a regular rate of flow with a reasonably fine adjustment to this rate. With such modification it has proved a simple and trouble-free apparatus for continuous intramuscular infusion.

The quantity of fluid used as the diluent for the twenty-four hour dose of penicillin is 500 mils. To maintain a regular flow this must be delivered at the rate of 0·3 ml per minute, and with a standard glass dripping chamber this quantity amounts to six drops per minute—too few for easy regulation. This has been overcome by the use of a fine hypodermic needle as the dripping agent. Such a needle delivers smaller drops and, as shown in Table I, provides a sufficient number of drops per cubic centimetre to permit easy visual adjustment.

TABLE I.
Relationship of Needle Calibre and Dripping Rate.

Needle and Dripper.	Number of Drops per Mil.	Rate per Minute to Deliver 500 Mils in Twenty-four Hours.
British Standard Whitworth gauge of needle:		
20	70	23
22	90	30
24	90	30
25	120	40
Glass dripper ..	18	6

Apparatus.

The apparatus consists of a "Soluvac" flask and giving set, in which is incorporated a needle of 22, 24 or 25 gauge (British Standard Whitworth gauge), and a piece of sponge rubber three inches square and one-half inch thick. Six inches are cut from the five-foot length of "Latex" tubing included in the set and attached to a metal connexion which fits through the rubber stopper of the flask. A screw clip is attached to this length, and subsequent adjustments of this clip are made easier if the thread is lightly covered with paraffin. The base of a hypodermic needle is forced into the lumen of the free end, so that the collar of the needle makes a water-tight joint with the inner surface of the tubing. The Murphy's dripper is then connected, with the shaft of the needle threaded through its end. Needles of this fine gauge are so short that if the dripper is used in the normal way the end of the needle will not project beyond the central glass stem, and fluid running through the needle coalesces in the stem to form the usual sized drop. Therefore, the dripper is connected reversed, so that the needle projects freely into it, and the glass stem is at the lower end. Solution passing from the needle forms a small pool at the bottom and overflows into the stem to fill the remainder of the system. The remaining 54 inches of tubing are attached to the dripper and joined to a standard intravenous needle. A variety of needles has been tried of different lengths and gauges, with and without lateral outlets cut into the shaft. All are satisfactory, provided that the penicillin solution is delivered deeply into the muscle and that movement of the needle in the tissues is minimized by firm fixation. The needle supplied in the giving set is 38 millimetres long and fits the tubing closely by means of an expanded corrugated end piece; it is quite adequate for general use.

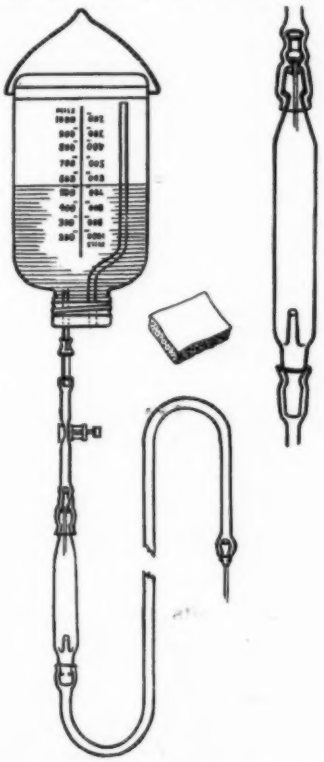

FIGURE I.
Apparatus for continuous intramuscular infusion, showing apparatus assembled, sponge rubber pad, and an enlargement of the dripping chamber.

Cleaning and Sterilization.

After each infusion the whole apparatus is washed through with a vigorous stream of distilled water. As the fluid is a simple mixture of saline solution and penicillin, prolonged boiling of tubing and glass in alkali is not required. It has been the practice to apply suction to the end of the delivery tube, with the apparatus attached first to a flask of distilled water for twenty minutes, and then to an air filter. After it has been thus washed and dried, sterilization is carried out by autoclaving. As a routine measure, both needles are cleaned with a stilette after each use. After repeated autoclaving the "Latex" rubber loses much of its elasticity and becomes sticky. when this occurs, the length between the metal connexion and dripper is best replaced, otherwise regulation with the screw clip becomes increasingly difficult.

Procedure.

Half the content of a litre flask of normal saline solution is discarded. The volume markings moulded onto the side of the flasks are sufficiently clear to allow this quantity to be poured off without other measurement. The dose of penicillin to be given in twenty-four hours is introduced into the remaining 500 mils. Such an amount is readily absorbed over that period and is insufficient to cause discomfort by virtue of the bulk of fluid injected. Muscle tissue appears to withstand concentrations of 200 to 400 units per mil of the purified preparations without the production of any irritative effect.

The lateral aspect of one thigh is shaved and the skin prepared with a volatile antiseptic. An area of skin and a track through subcutaneous tissues and fascia into the *vastus lateralis* are anæsthetized with procaine, the infusion apparatus is connected, and the system is filled. To minimize movement, the needle is plunged through the centre of the piece of sterilized sponge rubber and then inserted along the anæsthetized track. The rubber square acts as a wide collar, which may then be strapped firmly onto the thigh by strips of adhesive plaster nine inches long by one and a half inches wide. This measure serves to keep the needle firmly in position and to reduce movement by local fixation and "splinting" of the soft tissues. The needle has been inserted at right angles to the skin or with varying degrees of obliquity; no significant difference has been observed in comfort or reaction with these variations. The present practice is to insert the needle with the point passing distally, leaving an angle of approximately 60° open proximally.

The flask is then elevated until the level of fluid in the dripper is two feet above the infusion area. This gives an effective pressure head and ensures adequate flow, which is regulated by the screw clip. Fine adjustments to the rate may also be made by raising or lowering the flask.

Potency Loss.

In view of the emphasis which has been laid on the rapid loss of potency of penicillin in solution when kept at temperatures above 2° to 4° C., the following assays have been carried out.

Samples were taken from freshly mixed flasks containing a solution of sodium penicillin in normal saline solution and kept refrigerated. Further samples were collected from the last remnants in the flasks at the completion of

three infusions. The mean room temperature over these periods was 21·5° C. Each sample was assayed by the Oxford cup method on successive days, and the results are shown in Table II.

TABLE II.

Effect of Varying Periods at Room Temperature on Potency of Saline Solutions of Sodium Penicillin.

Specimen.	Hours at Room Temperature (21·5° C.).	Assay. (Units per Mil.)	
		Freshly Mixed.	After Period at Room Temperature.
A	25·5	150 140 135	160 145 130
B	33·0	140 120 115	130 120 115
C	23·75	315 280 270	250 240

Cowan[3] has reported that some types of rubber tubing may be destructive to the antibiotic power of these solutions to the extent of 25% to 50%. To assess the possible deleterious effect of the rubber tubing used in the apparatus, additional assays were made. From a freshly prepared solution of sodium penicillin in normal saline solution, a control sample was taken and kept refrigerated. A quantity of the same solution was introduced into lengths of both red rubber and "Latex" tubing, and these samples, together with a further control sample in a glass tube, were incubated at 37° C. for twenty-four hours and assayed. The "Latex" tubing was taken from a new "Soluvac" giving set and prepared by being boiled for twenty minutes in distilled water, dried and autoclaved. The red rubber tubing tested was ordinary surgical drain tube similarly prepared. The results are shown in Table III.

TABLE III.

Effect of Rubber Tubing on Potency of Saline Solutions of Penicillin at Body Temperature.

Specimen.	Assay. (Units per Mil.)
Control (2° C. to 5° C.) ..	130
Control (37° C.)	110
Red rubber tubing	125
"Latex" tubing	115

Within the limits of experimental error, the destruction of potency in these solutions is not significant either in the flasks at room temperature for twenty-four hours, or when the solution is in constant contact with the types of rubber tubing used at 37° C. for the same length of time.

Over the short period during which the solution is actually in contact with the tubing during the administration of an infusion, no detectable loss will occur.

Serum Penicillin Level.

The serum has been found to contain a constant bacteriostatic level of penicillin. Assays of this level have been made on 62 samples by means of a simple serial dilution method, modified from Rammelkamp[4] to produce a more complete grading of dilutions, and previously described.[5] Nutrient broth is prepared containing approximately 10,000 organisms per mil of a standard strain of *Streptococcus hæmolyticus* (N.R.R.L. 98) and 1% of washed human red blood cells. Dilutions of serum are made in this mixture and incubated for eighteen hours. Bacteriostasis is indicated by sedimentation of the red blood cells with a clear supernatant fluid. When complete bacteriostasis has not occurred, growth of the streptococcus causes hæmolysis of the red cells, thus providing an effective indicator; a sharp end-point is almost invariably obtained. The results of these assays are shown in Table IV.

TABLE IV.

Serum Levels with Varying Doses of Sodium Penicillin.

Dilutions of Serum Causing Complete Inhibition of Hæmolytic Streptococcus, 98.	Twenty-four-hour Dose of Penicillin.		
	100,000 Units.	150,000 Units.	200,000 Units.
Nil detected	7	—	—
1:1	5	3	—
1:2	6	9	2
1:3	3	5	2
1:4	—	—	—
1:6	—	—	14
1:8	—	—	3
1:12	—	—	3

Clinical Features.

Pain.

A feature of the intermittent administration of penicillin by three-hourly intramuscular injections is the psychological reaction of the patient to the frequent injections. When treatment extends over a week or longer, considerable distress is caused and the patient becomes apprehensive and progressively more disturbed as time goes on. There develops, in effect, a state of "needle shyness". This is of major concern at night time, and although the interruption of sleep is usually more apparent than real, the interference with rest acquires a disproportionately large significance in the patient's outlook.

By continued infusion these multiple needle pricks are avoided and those who have been receiving three-hourly injections, when transferred to the continuous method of administration, express relief at the undisturbed night's rest.

When a single intramuscular injection of two to four mils is given, the degree of pain and the general subjective symptoms vary greatly from patient to patient; but constantly some pain and "stiffness" persist for one to five minutes. When the continuous infusion was used there was less complaint, and in many cases in which a local reaction was absent, complete comfort has been achieved.

Nursing.

Many patients receiving penicillin are ambulatory. With continuous infusion they become confined to bed and require all the additional labour of nursing and feeding.

The apparatus is simple, but demands supervision every two or three hours to maintain a steady rate of flow. Movement of the patient in bed, or tangling of the delivery tube in the bed clothes or under the patient's body interferes with the rate. The cleaning, maintenance and sterilizing of the sets require extra work.

Reactions.

Reactions have occurred around the site of the infusion. The only factor that seems to be constant in their causation is movement of the needle in the tissues, with reflux of penicillin solution from the muscles into the subcutaneous tissues. The reactions have varied in degree, from a mild sensation of soreness and stiffness in the muscles to redness and brawny œdema of the limb, extending as far as six inches in all directions around the infusion site, and accompanied by a rise of temperature as high as 104° F. The time of onset of the reaction after the infusion is commenced is similarly variable; in some cases discomfort is experienced within twenty-four hours, and at thirty-six hours redness and swelling are apparent. In others the infusion has been continued for as long as 194 hours, and not even the slightest reaction has occurred. In those cases in which severe reactions have occurred, disability subsequently has been prolonged for periods up

to fourteen days, depending upon the severity of the reaction. The main complaint is of soreness, present whilst at rest and aggravated by movement. Tenderness, swelling and thickening of the tissue mass in the affected area are apparent.

In all, 257 flasks of penicillin have been administered; in no case has there been evidence of any infection due to Gram-negative or other organisms, or any sign of abscess formation.

An attempt has been made to determine what is the optimum period for which an intramuscular needle may remain *in situ* without fear of reaction. If the position of the needle is changed after every 500 mils (that is, approximately each twenty-four hours), no significant reaction occurs. If two flasks are administered over forty-eight hours through the same site, some reactions occur. Because of the unpredictable nature of these reactions, the best indication for withdrawing and reinserting the needle elsewhere would seem to be the onset of symptoms and signs in the infusion area. Once these are present they persist and increase in severity until the needle is removed.

Reports of Cases.

Trial of this method has been made in 72 cases, and the following case reports indicate the type of response obtained.

CASE XV.—At the age of thirteen years, this patient had suffered an acute hæmatogenous osteomyelitis of the right ilium. Metastatic infection also occurred at this time in his left ilium. After prolonged immobilization and multiple incisions the infection subsided, and for eight years he had been free of any disability. In late December, 1944, pain commenced in the upper part of the right thigh with some redness and swelling on the lateral aspect of the limb in its upper third, and mild fever. This subsided with rest in bed, but recurred soon after the patient began walking about. On this occasion, fever was more pronounced, the temperature rising to 102° F., and the cellulitic area was extensive. Radiological examination revealed an old osteomyelitis in the supraacetabular portion of the right ilium. The leg was immobilized in a Thomas splint with the foot fixed to a Sinclair's footpiece, and light traction was applied. The leucocytes numbered 18,600 per cubic millimetre. Penicillin, 200,000 units in 500 mils of normal saline solution, was given every twenty-four hours by continuous intramuscular infusion into the left thigh, and sulphathiazole, one gramme every four hours, was given by mouth. The fever was only partly controlled, and the temperature rose each evening to 101° F., and there was no change in the cellulitic area. Pain, however, disappeared rapidly, and the patient's general condition was excellent. The same treatment was continued for seven days, and assay of the serum sulphathiazole content showed a level of 5·8 milligrammes *per centum*. The combined bacteriostatic effect of the penicillin and sulphathiazole in the serum was repeatedly estimated and was shown to be sufficient to cause complete inhibition of the standard streptococcus in a dilution range of 1:6 to 1:12. After seven days' treatment, an incision was made on the lateral aspect of the right thigh below the great trochanter, and four ounces of pus were released from an abscess cavity extending proximally over the anterior surface of the hip joint. A pure growth of hæmolytic *Staphylococcus aureus* was obtained in culture from the pus. A penicillin tube was passed to the apex of the cavity, and the wound edges were lightly coapted by sutures. Within twelve hours the patient's temperature was normal, and it remained so thenceforth. Penicillin solution, in a strength of 250 units per ml., was instilled into the tube twice a day. The tube was removed on the eighth day after operation. The total dose of penicillin was 2,600,000 units given over a period of thirteen days. The initial infusion was administered into the left thigh for a period of 148 hours through the same needle, which was left undisturbed in the same position, as no trace of reaction occurred. After operation the infusion site was changed every forty-eight hours. The wound had healed completely two weeks after operation.

CASE XXXIII.—This patient was suffering from erysipelo-cellulitis of the face. Four days before his admission to hospital a small sore had appeared behind the lobe of the right ear. This subsided without treatment, but thirty-six hours later pain, swelling and redness appeared over the whole of the right cheek. For twelve hours he had been feeling ill, and he had had one shivering attack. On examination of the patient, pronounced erysipelo-cellulitis was present, extending across the whole of the right cheek up to the lower margin of the orbit, into the inner canthus, and across the bridge of the nose. The spreading edge was well marked and the whole affected area was deep red in colour and tensely hard to palpation. The patient's temperature was 102° F. The infection was obviously virulent and rapidly extending. The administration of penicillin was commenced immediately, 150,000 units in 500 mils of normal saline solution being given by continuous intramuscular infusion each day. After twenty-four hours, pain had entirely disappeared and the lesion was resolving, though the swelling was unchanged. The temperature had returned to normal. The penicillin therapy was discontinued after two flasks had been given, the total dose being 300,000 units. Considerable reaction occurred around the site of infusion, and "stiffness" persisted in the right thigh for six days after the infusion was discontinued. Convalescence was uneventful and the patient was discharged from hospital nine days after his admission.

CASE XLV.—The patient was suffering from chronic parotitis. He complained of chronic pain and swelling in the region of his left parotid gland, of four months' duration. The symptoms were constantly aggravated after a meal. When the patient was examined, a hard, tender mass was present in the left parotid region extending behind the angle of the jaw into the pterygoid region. The orifice of Stenson's duct was inflamed and œdematous, and mucopus was exuding from it. No calculus or other abnormality could be detected when the duct was probed, or by X-ray examination after lipiodol injection along the duct. Penicillin (100,000 units in 500 mils of normal saline solution) was given every twenty-four hours by continuous intramuscular infusion for four days. Within twelve hours there was considerable subjective improvement, with rapid relief of pain; after forty-eight hours appreciable reduction in swelling was apparent, and by this time the duct orifice was normal in appearance and was producing clear saliva only. The total dose of penicillin given was 400,000 units, and at the end of the infusion the parotid region was normal. The infusion site was changed every forty-eight hours. There had been no recrudescence when the patient was examined one month later.

CASE LII.—This was a case of lobar pneumonia. The patient had suffered severe pain in the lower part of the chest and the upper part of the abdomen on the left side for twenty-four hours; during this period he had become increasingly ill. A troublesome cough had also commenced, which produced a small amount of tenacious "rusty" sputum, and which aggravated his pain. On his admission to hospital, signs of consolidation were present over the lower lobe of the left lung; these signs were confirmed radiologically. The temperature was 104° F., and the leucocytes numbered 35,700 per cubic millimetre. Penicillin (100,000 units in 500 mils of normal saline solution) was administered every twenty-four hours by continuous intramuscular infusion. The patient's temperature was normal in thirty-six hours, and penicillin therapy was discontinued after seventy-two hours when a total of 300,000 units had been given. The needle was withdrawn and reinserted in a fresh position after forty-eight hours. Further convalescence was uneventful, and the patient was discharged from hospital, clinically and radiologically well, two weeks after his admission.

Discussion.

Various different methods of exhibiting penicillin are being reported, most of them directed at slowing either the rate of absorption or the rate of excretion, or both. The drug has been conjugated with human serum albumin[6] to form a large molecular complex, which on injection forms a depot of slowly released penicillin of unimpaired therapeutic efficiency. Its suspension in a base of oil, or oil containing up to 6% of beeswax, has also been tried.[7] Localized vasoconstriction in and around the area of administration may be produced by prolonged chilling[8] or by the addition of adrenaline[9] to the penicillin solution.

The formation of a "penicillin excretion barrier" by means of "Diodrast"[10] or para-amino hippuric acid[11] delays loss through the kidneys.

Appreciable serum levels and therapeutic effect have been observed when the drug was given by mouth, together with a suitable alkaline buffer such as trisodium citrate.[12] Little and Lumb[13] reported satisfactory blood levels when penicillin, which had been mixed with raw egg, was taken by mouth after a dose of sodium bicarbonate or magnesium trisilicate.

When a system of intermittent or continuous injection of a simple solution of penicillin is used, only one indisputable advantage is known to result from the latter method; when it is used the patient is spared multiple, slightly painful needle pricks. The question whether bacteriostatic power in the serum is improved by a constant but low penicillin titre as opposed to a regularly recurring rise and fall of this titre above and below such a level is still vexed. No positive evidence, either *in vitro* or *in vivo*, has yet been adduced to determine this point.[(3)(5)]

It has not been possible to assess the clinical results in this series of cases on a strictly controlled basis because of the diversity of conditions treated and the limited numbers. However, an attempt has been made to appraise critically the therapeutic effect in comparable cases in which equivalent dosages were given by both methods. In acute lesions and in those caused by the more sensitive types of organisms, the response achieved by both systems appears to have been equally rapid and complete. In more chronic types of infections the early subjective improvement, which constantly precedes objective relief, and the increased duration of the course of treatment necessary to produce complete cure have also been the same. In all groups of cases the basic criteria have been to remove nonviable tissue by releasing pus and sloughs or removing sequestra, and then to bring the drug into contact with the infecting organism in a sufficient concentration for a sufficient time; to achieve this, local treatment has often been used in addition to either form of parenteral therapy. This has further clouded the issue.

There is, therefore, no clear indication of any greater therapeutic efficiency in either method. It is considered that both methods are highly effective and that for general purposes the distinction between them in this regard is a fine one. Three-hourly injections giving a total dose of 120,000 to 160,000 units each day have been widely used and give what is now regarded as a full penicillin effect; the method is simple and requires no special facilities. Whatever inconvenience it causes is a small price to pay for the benefits it bestows. However, continuous intramuscular infusion appears to have a place in penicillin therapy, as it is constituted in its present stage of evolution; but its value is gauged on practical considerations only. To the gravely ill patient it grants welcome and perhaps necessary freedom from disturbance; to one undergoing prolonged treatment it gives periods of uninterrupted sleep and relief from apparently incessant injections. But it is subject to the inescapable demands associated with regulation of flow, cleansing, and sterilization, which are inherent in any transfusion apparatus and which may render its use in other than an institution a matter of some difficulty.

Summary.

A method of giving penicillin by continuous intramuscular infusion is described, with details of the apparatus and of its clinical use.

The effects on potency of temperature and of two types of rubber tubing were investigated, and no significant loss was detected.

A series of 72 patients was treated and 275 flasks of penicillin solution were used; the serum penicillin levels maintained during 62 infusions are recorded and brief clinical details of illustrative cases are given.

Reports of investigations into alternative ways of systemic administration of penicillin are enumerated, and the advantages and disadvantages of this particular method are discussed. It has proved simple and trouble-free in use, and is considered valuable in allowing the patient uninterrupted and undisturbed rest.

Acknowledgements.

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Reviews.

"STUDIES ON IMMUNISATION."

THERE seems to be no more reason for the publication of the second series of "Studies on Immunisation" by Sir Almroth Wright than there was for publishing the first series.[1] The motto of the book, "the physician of the future will be an immunisator", may have seemed not unlikely of fulfilment to such enthusiastic vaccinators as Wright in the first three decades of this century, but the successful search for antibacterial substances, for example, the sulphonamides and penicillin, has profoundly changed the whole picture. Any role of immunizator seems to have almost passed from the physician to the public health administrator and the Medical Corps of the armed services. And by a strange twist of fate it was in Wright's own laboratories that Fleming discovered the antibacterial action of *Penicillium notatum*.

This book is a reprint of old papers going back to 1910 and nearly all over twenty years old, and as they relate mostly to vaccine treatment and practical and theoretic considerations of immunity and immunization, from an epoch when chemotherapy was more a dream than an accomplishment, excepting Ehrlich and syphilis, the reader will find it difficult to sustain his interest. It belongs rather to the history of medicine. It is true that there is an appendix in which there are reprints of an old chapter on the treatment of pneumonia with optochin (1914), and of a paper on "Sanocrysin" in tuberculosis (1926). The work is beautifully printed and is adequately illustrated, including one coloured plate.

[1] "Studies on Immunisation: Second Series: With Appendices dealing with Anti-typhoid Inoculation, Chemo-therapy, and Statistical and other Operations of Induction", by Sir Almroth E. Wright, M.D., F.R.S.; 1944. London: William Heinemann (Medical Books) Limited. 9¾" × 7¼", pp. 262, with illustrations. Price: 25s. net.

The Medical Journal of Australia

SATURDAY, SEPTEMBER 15, 1945.

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Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

A PATHOLOGY SERVICE FOR NEW SOUTH WALES.

MEDICAL men and women know full well that the practice of medicine is both an art and a science. They also know that to practise the art and to ignore the science is just as foolish as to believe that science alone is sufficient equipment for the practitioner. History, as usual, shows forth the development of this fundamental conception. In the seventeenth century Thomas Sydenham recognized the need for a return to common sense and practical methods. He was "faithful to the true principles of Hippocrates" and he "brought medicine back to clinical observation and personal experience". And in our own day Sir Thomas Lewis, entering a successful plea for what he so aptly called clinical science, has pointed out that it includes human pathology and is fundamental to the proper pursuit of the healing arts. The duality of requirement—art and science—is nowadays realized as a rule by governments, by statutory bodies and by hospital boards who have to find the money for the setting up of scientific departments of medical inquiry. The cases in which scientific aids to medical diagnosis and treatment are not seen to be necessary must be very rare indeed. Failure, when it occurs, is in the full recognition of what is adequate and what is not. This is sometimes noticeable in regard to the provision of pathology services. The large areas that have to be covered in country practices in Australia complicate this matter, as they do many other problems connected with medical practice. Medical practitioners, especially in the country, can and do undertake to their own satisfaction a good deal of pathological investigation; but many of them are too occupied with other matters to do much laboratory work, and in any case many procedures are beyond the scope of the general practitioner or are more efficiently carried out by a specially trained pathologist. In passing it should be remarked that Australia is not alone in her need for increased diagnostic facilities. In the *Canadian Journal of Public Health* for April, 1945, plans are set out for the establishment of adequate diagnostic services (radiological, pathological and bacteriological) at hospitals throughout the Province of Manitoba; legislation will shortly be submitted to Parliament, and is expected to be passed. The present object is to direct attention to recommendations that have been drawn up by the Section of Pathology and Bacteriology of the New South Wales Branch of the British Medical Association for the establishment of a comprehensive pathology service for the State.

The first recommendation is that a survey should be made of the needs for medical services including the requirements for diagnostic facilities.

On the result of the survey, recommendation should be made for the establishment of additional laboratories, and their location should be indicated. The site of such proposed laboratories should be determined in relationship to the immediate population of the vicinity, of the population within a working radius, on accessibility as regards transport, and in thickly populated areas as regards proximity to large general hospitals. The laboratories should be established in hospitals which provide, or will be equipped to provide, all other necessary auxiliary medical services.

Any hospital that is fully equipped to cover adequately the investigation and treatment of patients is called a base hospital. It is held that base hospitals should be established to serve adequate areas, and that in places where base hospitals are projected but not yet in existence, the laboratory should be temporarily located at the existing hospital and should be adequately equipped and staffed. When the survey has been made, it is recommended that the staffing requirements should be ascertained. "Certain laboratories would require a complete 'staff' unit, others might require technical staff *plus* a visiting qualified pathologist." It is suggested that a Pathology Advisory Committee should be created and that its personnel should be as follows: one representative appointed by the University of Sydney; two representatives appointed by the New South Wales Branch of the British Medical Association, one of whom shall be a practising pathologist and one a full-time hospital pathologist, appointed every three years; the committee should have power to coopt, as required, a graduate in science and/or a representative of the Society of Technicians; the secretary of the Section of Pathology, it is thought, should be a member of the committee *ex officio* and might also be secretary of the Advisory Committee. The design of laboratory buildings and the accommodation, according to the recommendations, are to be approved by the Advisory Committee. The committee should also approve laboratory equipment which would be obtained from a Central Equipment Store. A first-rate recommendation is that steps should be taken for arrangements to persuade the army to make its pathology equipment available to the central store as soon as possible after the cessation of hostilities. For base hospital laboratories it is held that the staff should comprise medical graduates, science graduates and a technical staff. A fully qualified medical graduate is suggested as officer-in-charge of each laboratory, with medical assistance, should it be necessary. This officer should be responsible for the efficiency of the department and for all reports issued from it. It is thought that he should be regarded as having a status equal to that of a member of the honorary staff and be *ex officio* a member of the medical staff board of the hospital. He should also be

allowed the right of private practice and the right to charge fees for laboratory service to private and intermediate patients in the hospitals to which he is attached. The salary suggested for his services to the hospital is a commencing salary of not less than £800 *per annum*. It is suggested that graduates in science should be employed where special work such as biochemical work warrants their employment, and also that a competent and adequate lay technical staff should be attached to each laboratory. The minimal technical staff is thought to be one trained technician holding the certificate (medical) of the Society of Laboratory Technicians of Australia and one junior technician. Reading these recommendations, we at once recall a statement made in 1940 in an address by Professor W. K. Inglis. (See THE MEDICAL JOURNAL OF AUSTRALIA, May 4, 1940, page 609.) He said that:

> A well-trained pathologist endowed with the true scientific spirit, one who can win the confidence of his clinical brethren, will prove to be a boon to any group of practitioners. In competition with none of them, he can, in his special field, be adviser to them all. If he is of the right calibre he will bring an interest into their work such as they never dreamed of, and, should there be some who feel overburdened with monotonous routine, he may save them from becoming mere carpenters and pillmongers of the profession.

The recommendations made by the Section of Pathology and Bacteriology deal with a comprehensive pathology service for New South Wales. They do not therefore touch only base hospitals and other hospitals of that type. They cover also teaching hospitals and "public hospitals with large pavilions". The recommendations in regard to these are as follow:

1. Full-time pathologists should receive an adequate salary. These will be senior men or men with more than average ability who choose to specialize. A minimum salary of £1,500 *per annum* is recommended. It is recommended that such full-time pathologists should have the status and privileges of the honorary medical staff, but as full-time officers of the hospital they should confine their services to the public hospital patients.

2. The pathology work on private and intermediate patients in private pavilions attached to public hospitals should be carried out either by (*a*) part-time pathologists, either honorary or receiving remuneration from the hospital, or (*b*) by any pathologist carrying on the speciality of pathology.

3. Relation of full-time pathologists to research: All large public hospitals should raise their pathology department to the dignity of an institute with a medical director and adequate facilities for research. The full-time graduate laboratory staff should be encouraged to interest themselves in research and should be relieved of routine to an extent that provides adequate opportunity for research.

The final section of the report contains recommendations regarding higher education and research; they will be considered on another occasion. In regard to the recommendations to ensure a comprehensive pathology service for New South Wales, the Section of Pathology and Bacteriology of the New South Wales Branch is making an attempt to give effect to the views of the Federal Council for the provision of complete diagnostic facilities in medical practice. A subcommittee has been appointed to discuss the recommendations with the appropriate authorities. Should the recommendations be carried into effect—and there seems to be no reason why they should not—there can be no doubt that the quality of medical work in the areas of their operations will be improved. Professor Inglis spoke of a renewed interest and in certain circumstances the forsaking of a dull routine. This will mean that an infusion of the spirit of science has begun. Of this Professor Inglis wrote:

> The spirit of science is elusive and as light as thistledown; it is not to be hunted with a bludgeon, it is to be wooed as the poet's muse. Should it find its way into the scientific departments of an institution, there is no limit to the influence it may have. The spirit of science ennobles as no baser passion can, and its light touch may transform the laboured efforts of routine service into a life dedicated to that noblest of all quests, the search after truth for its own sake.

Current Comment.

ROAD SAFETY AND MOTOR CAR DESIGN.

At the present time the motoring public has its attention well focused on the post-war motor car, and much speculation is abroad concerning new items of equipment that may be incorporated in it. Medical practitioners have a twofold interest in the matter; in the first place, as motorists themselves, they will welcome any improvements in motor cars that will add to the ease and comfort of driving them; in the second place, they have a professional concern with safety on the road and the avoidance of damage to human beings. J. F. Bramley, Safety and Welfare Superintendent of the Austin Motor Company, and N. T. Glynn, Medical Officer to the Austin Motor Company, have made a contribution to the question of improvements in motor car design as an aid to safer driving.[1] They consider the matter under the headings of control, stability, vision, and comfort factors. Proper control, they hold, is the result of satisfactory steering equipment, efficient brakes and the facility of prompt acceleration. They point out that, although a minimum of three pedals seems necessary for the control of a motor vehicle, the driver unfortunately has only two feet. If a single pedal could be in some way made to operate both accelerator and brake, an awkward time-lag would be eliminated. On the subject of brakes, Bramley and Glynn have a word to say in condemnation of the type of brake drum which admits water and becomes inefficient for some time after a hosing or after the vehicle has been driven through water. They also point out that even the good brakes on modern motor cars become inefficient if they are not properly cared for. Modern steering equipment, they believe, is so good that little improvement is needed. Turning to the question of stability, the authors point out that it depends primarily upon good springing and low centre of gravity in relation to the breadth of the wheel track. Steering is also concerned during cornering. They think that more than the present amount of attention should be given to the design of springing. With regard to vision, the authors assert that the driver needs a clear, uninterrupted view in front of him and for nearly 90° to the right and left. Further, the closer to his front wheels the road is visible, the better. They recommend the double windscreen wiper and a defrosting device; the latter need hardly be considered in most parts of Australia. They believe that insufficient attention has been paid to the front pillar as an obstruction to the driver's view; this, they hold, is a frequent cause of collisions at crossroads. Such blind spots should be eliminated, even if this means a reduction in the strength of the roof. Safety glass has almost invariably been incorporated in motor vehicles for some time past. Discussing the possible use of plastics instead of glass, as in aircraft, Bramley and Glynn point out that these substances at present have the disadvantage of being easily abraded by dust. However, if a suitable plastic was developed, it might be possible with it to produce curved transparent surfaces and thus again greatly improve the driver's vision. For rear vision, they incline to the view that the outside mirror is the best device, as it is not affected by the size and position of the rear window or by the pulling down of the rear blind. With regard to seat level, the authors state that "the tendency for seats to get lower, bonnets longer, and screen rails higher, can be said to have

[1] *The Practitioner*, April, 1945.

reached its limit in 1937". We recollect a certain type of light car, the bonnet of which was so long, and the windscreen of which was so shallow, that the driver, when ascending a steep hill, had within the range of his vision nothing but the heavens; perhaps there was something symbolic about this arrangement. While the rear engine layout has been suggested as an improvement, Bramley and Glynn believe that the best examples of driving visibility in the conventional motor cars of the present day are good enough for all practical purposes. But they think that the driver's seat should be adjustable in the vertical as well as in the horizontal plane. At night the question of dazzle, although important, is much less so than that of inadequate lighting. Possibly future investigations will proceed on the lines of devising reflectors and lamp glasses which will combine good, even spread with adequate forward range, whilst avoiding directly dazzling beams of light. The authors recommend standardization of size, power and height of headlamps as a means of solving this problem.

The chief comfort factors concerned are seating and ventilation. In the opinion of Bramley and Glynn the ideal seat should slope downwards from front to rear at an angle of about 10°, and the back should make with it an angle a little greater than a right angle. The back should be sufficiently high to support the shoulders, and should have no pronounced concavity, so that the driver may ease himself by slight changes of position. Bucket seats are not a good idea—the driver fits into such a seat "like a snail into his shell". The seat should also be deep enough to support the thighs almost to the bend of the knee, and high enough, when the feet are on the pedals, to allow the legs to be at an angle nearer the vertical than the horizontal. The very low seat gives poor vision and keeps the hamstrings stretched in a tiring way. Ventilation also should be adequate; some provision should be made for changing the air inside the motor car body, since gases which escape into the bonnet are bound to enter the body. Toxic effects from exhaust gases upon the nervous system may vary from those which are not noticed, but may impair efficiency, to those which last for weeks. Air-conditioning in the motor cars of the future would be the answer to the problem.

In a concluding paragraph, Bramley and Glynn make some suggestions for measures to mitigate the effects of road accidents, which are bound to occur in spite of all precautions. The first obvious step, they state, is the elimination of certain dangerous mascots, some of which have already been forbidden. Club badges, if they must be carried, should be mounted flat on the radiator grille, and not on the bumper bar or the top of the bonnet. The completely streamlined car would seem to be the safest; even a side lamp mounted above the wing, and not in it, might prove to be a lethal weapon, and door handles should be recessed and hinges concealed. From the inside of the body should be eliminated all hard knobs that might cause injury to driver or passenger. The fitting of steering wheels with flexible spokes and rim would lessen the risk of the driver's suffering rupture of an abdominal organ in an accident. Bramley and Glynn, who are in a position to understand the matters on which they write, have presented a useful and practical paper. It will be interesting to see how the motor cars which are at present in the embryonic stage will compare after delivery with those envisaged by the authors.

BRONCHIAL ADENOMA.

A SYMPOSIUM on the subject of the so-called bronchial adenoma at the twenty-fifth annual meeting of the American Association for Thoracic Surgery, held at Chicago in 1944, shows that there is still room for controversy as to the malignancy or otherwise of these tumours and as to the bearing of this malignancy or lack of it on their management.[1] On the one hand it is pointed out that the tumours are often known to have been present for many years and that patients often remain well for many years after the removal of one of the tumours through the bronchoscope. On the other hand it is pointed out that there have been numerous reports of the metastasis of tumours thought to be adenomatous and also of their having suddenly begun to grow rapidly. C. L. Jackson, F. W. Konzelmann and C. M. Norris, who discuss the clinical features of twenty such tumours on the basis of observations, some of which extend over periods of ten years or more, state that they do not believe that the tumours have any inherent tendency towards malignancy. They recognize the possibility of extrabronchial growth of the adenoma, producing a lesion shaped like a collar stud with the larger part outside the bronchus, but they think that this possibility is sometimes over-emphasized. These writers favour bronchoscopic treatment, except when the size of the tumour is too great for its accomplishment or when serious permanent disease is present in the lung distal to the tumour. J. M. Chamberlain and J. M. Gordon, on the other hand, regard pulmonary resection as the treatment of choice, because it offers a definitive cure, because the hazards associated with the damaged lung distal to the tumour are avoided and because of the possibility of malignancy. E. A. Graham and N. A. Womack go further and state that in their opinion attempts at local removal through the bronchoscope are unwise and dangerous and that total pneumonectomy is the procedure of choice; they point out that it is frequently impossible to determine from a biopsy specimen whether or not a particular tumour has already become malignant.

Evidently much depends upon what is one's definition of malignancy. Graham follows Virchow in regarding invasion as the criterion of malignancy. He draws attention to the superficial resemblance of the bronchial adenoma to the mixed tumours of the salivary glands which often exist for long periods before exhibiting invasive qualities, and he adds: "Of course, these tumours are not all malignant when first seen . . . they are potentially malignant." The controversy is somewhat reminiscent of that which used to take place, whether certain kinds of gastric ulcer were potentially malignant. However it may be resolved in the future, there is no doubt that when one of these tumours is found or thought to be present, a piece of it should be removed through the bronchoscope for histological examination before definitive treatment is undertaken. In the course of this procedure the operator may be able to decide whether he could remove the whole tumour through the bronchoscope. It was made clear by several contributors to the symposium that bronchoscopic interventions sometimes cause furious and even "frightful" bleeding, a contingency for which bronchoscopists henceforth will doubtless not be unprepared. No mention was made by any of the contributors of the implantation of radon into the bronchial adenoma or its base after removal; such an uncertain procedure, though rendered out of date by recent advances in surgery, might still be justified when the tumour could not be removed through the bronchoscope, yet the patient was too ill to undergo an operation for pulmonary resection.

[1] *The Journal of Thoracic Surgery*, April, 1945.

THE HALF-YEARLY INDEX TO "THE MEDICAL JOURNAL OF AUSTRALIA".

THE index for the first volume of this journal for 1945 (January to June) has now been published. Copies will be posted to those who have previously asked to have their names put on the index list. A copy of the index is sent to all libraries, medical societies and associations, as well as to journals having exchange arrangements with THE MEDICAL JOURNAL OF AUSTRALIA—there is no need for these bodies to ask that a copy should be sent. Other readers wishing to receive a copy are asked to write to the manager at the office of the journal, The Printing House, Seamer Street, Glebe, New South Wales.

Abstracts from Medical Literature.

SURGERY.

Chest Wounds in Pacific Jungle Warfare.

CAPTAIN H. G. HARDT, junior (*Archives of Surgery*, December, 1944), reviews thirty-two cases of chest wounds sustained during jungle warfare. The missiles responsible were mortar-shell fragments most commonly and rifle and machine-gun bullets. Knife and bayonet wounds of the chest were not encountered in this series. The author emphasizes that the character, clinical course and end-results of penetrating war wounds of the chest are influenced by three general factors: the size, irregularity, course and velocity of the projectile, the general physical condition of the soldier when wounded, and the promptness of first aid and of adequate hospital treatment. All the men in the series reviewed were seasoned troops in good general physical condition. Early and adequate medical care for penetrating thoraco-pulmonary wounds is vital to the welfare of the patient. In this regard the present series of patients was well served. Many reached the hospital within one hour of being wounded, and only a single patient was delayed more than four hours. At this hospital was a team trained in thoracic surgery, and adequate facilities. Evacuation was by air over approximately 900 miles, during one portion of which distance an altitude of 9,000 feet was usually attained. Seven patients admitted some increase in dyspnœa at high altitudes, but only one required oxygen, and no untoward effects were observed. First-aid treatment consisted in the application locally of sulphanilamide and a dry dressing. Because they reached hospital so soon almost every patient was subjected to *débridement* and exploration. In seven cases a sucking pneumothorax was closed. Whenever extensive pulmonary damage or profuse bleeding was suspected the pleural cavity was explored. Sulphanilamide was applied locally, and the majority of wounds were packed with petrolatum gauze and left open. The following routine was observed in the treatment of hæmothorax. Aspiration and air replacement were used during the first seventy-two hours if dyspnœa occurred or continued bleeding from the lung parenchyma was suspected. Diagnostic aspirations were performed frequently. Asymptomatic hæmothorax was left undisturbed. Plasma given early proved to be a potent prophylactic factor in decreasing shock.

Immersion Foot.

A. LESSER (*Annals of Surgery*, March, 1945) has had the opportunity of observing over the past two years 52 patients suffering from immersion foot. Of the cases, 25 were acute, and the patients were admitted to hospital with varying degrees of sepsis and gangrene of the feet following combat duty some three weeks previously on the island of Attu. The other group of 27 were patients complaining of delayed disturbances of the feet coming on some six months after the same campaign. In the first group, the men were specially selected and in excellent physical condition. They wore two pairs of socks, one woollen, and leather boots which reached to about four inches below the knees, some having rubber soles. A group of ten patients who had the most severe lesions had arrived on Attu by submarine and had had no opportunity to change socks or boots for four days prior to the landing and for an average of six days afterwards. The other fifteen men of the first group had arrived by transport and had been able to change footwear up to the time of landing, and averaged only three to six days without changing during the subsequent fighting. These had milder lesions. All these 25 men had landed as an advance group, and their feet and legs had become wet immediately. It was necessary for them to abandon all equipment on making contact with the enemy, with the result that they were all practically without food for an average of six days. Temperatures averaged 35° F. with constant fog. They lay in ravines, gullies and foxholes without active movement for long periods, their feet and legs usually immersed in cold water from the melting snow. Except for an hour or two, physical rest or sleep was impossible. These men had little pain in their feet, and usually complained only of some numbness and discomfort until they came out of action and their boots were removed. Some men had battle wounds and three had lost large amounts of blood. As soon as their boots and socks were removed, extreme swelling and pain in the feet occurred. Gangrene, first dry, then septic, set in. Immediate treatment was by general warmth, warm food and drinks; morphine was given for pain, and in some cases, plasma transfusions. Sulphonamide drugs were used locally on the feet and also by mouth. Later treatment was by blood transfusions, iron, vitamin therapy, and a high Calorie diet. The foot condition varied from some forms in which there was no tissue loss, through others in which spontaneous separation of superficial tissues took place, to yet others in which large areas of soft tissue and bone necrosed and needed surgical removal, sometimes with later plastic revision. It was noted that arterial pulsations were good and that there was little elevation ischæmia, though dependency caused considerable bluish mottling of the skin of the feet. All wounds healed, and patients had remarkably little or no discomfort on walking, provided they were fitted with correct shoes and necessary supports. In only two cases were severe vasomotor disturbances seen, and these responded well to lumbar sympathectomy. In the second group of 27 delayed cases, the majority of patients complained of aching burning pain in the toes, and of sweating and cold clamminess of the feet. Temporary lumbar sympathetic blocks were performed with varying degrees of relief of symptoms. Some patients had moderate rigidity of the toes with gradual development of claw-foot deformities. Three patients were treated by lumbar sympathectomy with some relief of symptoms and a lessening of the sweating and clamminess, but there was a tendency for the aching pain to recur later. Microscopic sections of tissues removed from patients in the early and late stages showed a marked generalized fibrosis and collagen deposition, small blood vessels and nerves being embedded in the dense fibrous and collagenous material. Vessels showed extensive endothelial proliferation. There was inflammatory round cell and plasma cell infiltration of perivascular spaces. The factors producing this condition appear to be an increased susceptibility to low temperatures due to increased conductivity of the wet skin, associated with vascular stasis due to the prolonged immobility. In addition there is the effect on capillary permeability of hypoproteinæmia and hypovitaminosis due to lack of food. Blood loss will accentuate these factors. After the removal of the boots the tissues become flooded and choked with tissue fluids leading to thrombosis of small vessels and gangrene. The general fibrosis which follows leads to contractures, and perineural fibrosis causes the pain. These considerations suggest that treatment should be immediate elevation of the legs, with application, as soon as boots are removed, of pressure dressings to control exudate. These dressings may take the form of bandages of various types, Unna's paste boots, or possibly light plaster encasement. Local applications of cold rather than heat should be used. Intravenous administration of hypertonic agents such as plasma will correct the osmotic balance and tend to prevent exudation. Vasoconstrictor tone may possibly be influenced by adrenaline.

Gastric Resection for Duodenal Ulcer.

R. LEWISOHN (*Surgery, Gynecology and Obstetrics*, April, 1945), writing from the Mount Sinai Hospital group for gastro-enterological surgery, notes that it is now twenty-two years since this group began to abandon the operation of gastro-enterostomy in favour of gastric resection for duodenal ulcer. In the opinion of the author, not more than about 20% of patients with duodenal ulcer are permanently freed of symptoms by gastro-enterostomy. In 1916, Bland-Sutton pointed out that in the presence of an open pylorus, gastro-enterostomy would not cure a duodenal ulcer. He had gradually abandoned the operation in favour of a resection of the pylorus and of the portion of the duodenum containing the ulcer. In subsequent years, the scope of the operation was extended when it was found that in order to reduce the gastric acidity, it was necessary to remove a considerable portion of the stomach, at least one-half, the point of division extending to beyond the reentrant angle. The operation has become well established, but in recent years the author has found that certain small groups of surgeons are resistant to this advance, and are still recommending gastro-enterostomy for duodenal ulcer. Included in these are Trimble and Reeves, who in 1936 stated that gastro-enterostomy should be applied to the majority of these lesions, and that it was one of the most satisfactory operations in the armamentarium of the surgeon. More recently, Heuer made a study of the gastric and duodenal ulcers at the New York Hospital, and came to the conclusion that gastro-enterostomy was a satisfactory operation not only for duodenal ulcer but even for gastric ulcer. The author attacks these opinions. It is most difficult to evaluate the results of an operation unless the follow-up is done

most meticulously by personal interview. In any case, there is so much variation in individual technique, that results may not be comparable. In one school, only patients with simple lesions may be subjected to gastric resection, whereas in a school with more highly trained surgeons, a higher percentage of patients may undergo this type of operation. Some years ago a very careful follow-up of five to ten year results was made at the Mount Sinai Hospital, and it was found that 34% of patients who had had a gastro-enterostomy were then suffering from gastro-jejunal ulcer, 18% being proved definitely by reoperation. Mage, reviewing the material at the same hospital for the years 1923 to 1940, when gastric resection had almost replaced anastomosis, found that 2·5% of these patients were proved at reoperation to have developed gastro-jejunal ulcer, and another 5·5% had symptoms suggestive of this lesion. However, he had included in the 5·5% seven cases of gross painless hæmorrhage with normal X-ray findings, in which the patients may not have had gastro-jejunal ulcers at all. Even so, the incidence is markedly reduced compared with that following gastro-enterostomy. In good clinics, too, the immediate mortality from gastric resection should not exceed that following gastro-enterostomy. The surgeons at the Lahey Clinic hardly ever used gastro-enterostomy in the treatment of duodenal ulcer. They have reported 235 consecutive gastric resections for various types of peptic ulcer with 2·7% mortality. The mortality among the duodenal ulcer patients was only 3%. Wilson has reported 250 gastric resections with a mortality rate of 2·8%. Koennecke has published details of 468 resections with a mortality of 1·5%. The average mortality for gastro-enterostomy is in the region of 2%.

Disability after Head Injury.

D. DENNY-BROWN (*The Journal of the American Medical Association*, February 24, 1945) discusses the relationship between the degree of initial damage to the cranium and the extent of the subsequent symptoms. Great difficulty is encountered in the forming of an estimate of the degree to which direct physical effects account for disability after head injury. Still more obscure is the relationship between physical injury and the general symptoms such as headache and dizziness, intellectual impairment, psychoneurosis and changes in character and personality. The author analysed 430 consecutive patients admitted to the Boston City Hospital; he excluded patients under fifteen and over fifty-five years of age and also vagrant and alcoholic types. Follow-up for six months was carried out. Each patient was examined soon after admission to hospital by a team which included neurologists, psychometrists, psychiatrists, and electroencephalographer and social workers. The examinations were repeated at appropriate intervals. Generally the factors of prognostic importance can be arranged in two chief groups, those indicative of injury to the brain and those related to the environment. In the latter the author places the sources of anxiety derived from the injury, which predicate compensation, and the circumstances and duration of convalescence, which breed anxiety as to personal or family security. The insignificant part played by impaired intellectual function as shown by performance tests and intelligence tests calls for special comment. Persistent mental slowing was seen in two patients with ultimate recovery. In the best examples of cerebral laceration in the series the patients made remarkable recovery in all performance tests. The conclusion also throws doubt on the possibility that trauma alone may induce persistent dementia in a healthy brain. Occupational difficulties are as important as those related to compensation. The extensive association between head injury and psychiatric factors indicates great possibilities for the lessening of disability by psychiatric treatment.

The Importance of Protein Intake in Cancer.

H. C. CONNELL (*Canadian Medical Association Journal*, January, 1945) reports the effects of underfeeding on laboratory animals with cancer. He recalls that Galen mentioned the effects of underfeeding on tumours, and gives many references to work showing the retarding influence of diet restriction. Some workers have even found that prolonged reduced post-operative feeding reduces the frequency of recurrence of spontaneous tumours in mice. The author quotes the work of Tannenbaum, who in 1940 reviewed insurance statistics, and showed that persons of average weight or less are not so likely to develop cancer as those who are overweight. The author used mice with sarcoma transplants, and divided them into two series (of twenty animals each) as nearly similar as possible as regards age, sex and size of tumour. One series was fed a diet with low protein content, deficient in certain essential amino acids, while the control series received an ordinary diet. The results are given in detail, and show that tumour growth was over twice as rapid in the control series. One spontaneous recovery occurred in the control series to five in the underfed group. At the end of the experimental period the control group was mostly moribund, while all the animals on restricted protein intake appeared active. The author concludes from this and the other experimental evidence that protein intake is of very real importance in malignant disease.

Congenital Absence of the Gall-Bladder.

C. F. DIXON AND A. L. LICHTMAN (*Surgery*, January, 1945) review the literature on the subject of congenital absence of the gall-bladder, and add ten cases which have been observed at the Mayo Clinic. In the literature, they found thirty cases which had been reported prior to 1900 and fifty reported since that date. Generally speaking, much fuller data were available concerning this last group of cases, and the discussion centres mainly round these and the ten additional cases from the Mayo Clinic. The gall-bladder has been said to be absent in twenty-six species of mammals, seventeen species of fish and nine species of birds. It is of interest to note that, with the exception of the pilot whale, the mammals which do not have a gall-bladder are predominantly vegetarian and depend on ingested carbohydrate for their body fat. In the sixty cases mainly discussed, the anomaly was found at necropsy in twenty-six and at operation in thirty-four, the operation being performed in twenty-four of these cases because of symptoms suggestive of cholecystic disease. The average age of the patients was 46·7 years. In the group of patients over forty-five years of age, no less than 73% were suffering from symptoms similar to those of cholecystitis. The question arises as to how much the symptoms of gall-bladder disease are caused by disease or functional disturbances in the common bile duct or the sphincters rather than by the disease in the gall-bladder itself. However, the fact is that in most cases when the gall-bladder has been removed the symptoms clear up completely. But in the few cases in which the "post-cholecystectomy syndrome" occurs, these symptoms too are similar to those seen in the cases of absent gall-bladder. It has been shown that in animals which do not have a gall-bladder, bile is expressed from the sphincter in an intermittent trickle, while in those with a gall-bladder it is expressed in spurts at the proper stimulus. It may be that the presence of a functioning gall-bladder maintains a certain intraductal pressure while the sphincter is open, thus preventing regurgitation of duodenal contents. Jaundice was present in 48% of the sixty cases, stones being present in 27%, pancreatitis in 18%, and hepatitis to naked-eye examination in 8%. In 32% the common bile duct was dilated. In reviewing the treatment of these sixty cases, the authors point out that in twelve of them the common bile duct was drained for a prolonged period, in some of them in spite of the fact that there was no dilatation of the duct or stone formation. Of these twelve patients, ten had complete relief of symptoms. In one of the Mayo Clinic cases drainage of the duct was performed by a T-tube for a period of two years, the tube being eventually removed after progressive slow clamping of the tube without symptoms being produced. A year later the patient was still free of symptoms. Similar experience has been observed in the treatment of the "post-cholecystectomy syndrome" by the same method. It is suggested that this is the correct treatment for all cases of congenital absence of the gall-bladder with symptoms resembling those of cholecystitis, whether the common bile duct is dilated or not, and whether there is stone formation or not.

An Unusual Type of Varicose Veins.

W. H. PRIOLEAU (*Surgery*, January, 1945) draws attention to the fact that all varicose veins of the lower limb do not originate in disease of the saphenous veins. He reports a case in which there were very extensive varicosities of the thigh and leg; they originated in the inferior gluteal vein, which is a tributary of the internal iliac vein. In the case recorded, the varicosities had been present since the patient's childhood, and there were no other pathological findings, suggesting that the condition was congenital. Ligature at the gluteal fold and injection followed later by local injection of some remaining varicosities resulted in a disappearance of the symptoms. In the recent literature the author could find no reference to varicosities originating in the inferior gluteal vein.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held on July 4, 1945, at the Medical Society Hall, East Melbourne, DR. JOHN DALE, the President, in the chair. The meeting took the form of a symposium on alcohol.

Symposium on Alcohol.

DR. F. H. SHAW, lecturer in pharmacology, University of Melbourne, discussed the physiological effects of alcohol. Dr. Shaw said that alcohol was always treated in text-books of pharmacology as the type substance of central nervous system depressants. While there had been great advances in other branches of pharmacology and therapeutics, these surges had left almost untouched the narcotics and anæsthetics. It might be said that the empirical stage of pharmacology had almost ended. The next advance must come from a study of the mechanism of drug action. No further study of the action of ether or quinine along classical lines would prevent anæsthetic accidents or malarial relapses. It was necessary now to find out how narcotics affected the unit of life—the cell. Despite great advances in general physiology in the structure of the cell—especially its membrane—it was not known how alcohol affected the cell. Little advance had been made on the original Myer-Overton theory of solubility-partition coefficient, a theory propounded at the turn of the century. It was accordingly with great regret that Dr. Shaw could only refresh the memories of those present with a string of facts, to which he hoped to add an occasional novelty.

Discussing absorption, Dr. Shaw said that of an ordinary dose—30 mils of absolute alcohol—about one-quarter was absorbed in the stomach and the remainder in the upper part of the small intestine. Concentrated solutions might irritate the duodenum and delay emptying of the stomach and so absorption. Food also delayed absorption of alcohol, especially fats and milk. Alcohol then passed into the blood stream and distributed itself throughout the body water. The kidneys could not concentrate alcohol, and urine concentration was the same as plasma. It had been suggested that urine concentration should be used instead of plasma level as an indication of extent of intake, but careful experiments showed that that parallelism was not sufficiently exact. Alcohol was oxidized in the body, and the rate was constant and unaffected by concentration; this was rather unusual The rate was 2·5 milligrammes per kilogram per minute.

Referring to blood level, Dr. Shaw said that legal tests for drunkenness in some countries necessitated measurement of the amount of alcohol in the plasma. The effect of alcohol varied, owing to individual variation. The following figures were generally accepted:

0·025% to 0·1% ..... euphoria; impaired speech
0·1% to 0·2% ... disorder; speech movement affected
0·2% to 0·4% ..... drunk; gross inaccuracy
0·5% ..... coma

In testing the action of alcohol on the central nervous system, one entered the realm of psychology. Speed and accuracy were diminished; 30 mils of absolute alcohol were sufficient to show this. A moderate dose usually made one an extrovert. The University of Chicago investigation of beer in 1934 illustrated the difference between individuals. Thirty-six subjects were taken, and the tests used were the Romberg (equilibrium) test, the pricking test, and the response to red and green lights. The unit of dosage was the customary "bottle" of 3·2% strength (350 mils to 13 mils of alcohol). The following results were obtained: two bottles in fifteen minutes produced no effects; four bottles in thirty minutes affected five subjects in 69 tests, causing loss of motor control; eight to fourteen bottles in three and a half hours produced poor performances in all tests; of twelve subjects, eleven showed altered behaviour and eight vomited. Of 170 published papers on psychological experiments, all concurred that the effects of alcohol were purely depressant.

Dr. Shaw then discussed the effects of alcohol. He said that (i) alcohol was antipyretic, (ii) it depressed the heat-regulating centre, and (iii) it caused dilatation of the skin vessels. The use of alcohol in conditions of exposure was justified only if the patient had been removed to warm surroundings. There were three conditions—heat stroke, cold and shock—in which the administration of alcohol was a serious fault. In the first this was so because alcohol lessened the effectiveness of the regulation against over-heating, probably through the nerve centres, for the temperature remained high in spite of hydrotherapy. In the second, it was because of the increase of heat loss, the impairment of the regulation centre and the reduction of muscle activity and therefore of metabolism. In the third, the effects on the peripheral blood vessels and the distribution of fluids, as well as the unsatisfactory cardiac response, contraindicated its use.

Discussing circulation and respiration, Dr. Shaw said that the popular belief was that alcohol was a stimulant; but when it was used directly, this was not so. Indirectly, if alcohol was taken in strong concentration, by stimulating sensory nerves in the mouth and stomach it might reflexly accelerate the pulse rate. It might also increase pulmonary ventilation, because the carbon dioxide content in the alveolar air might fall. Finally, the mechanism, its extent and its value were doubtful.

Alcohol as a food provided energy, but no building material for restoration of tissues. It was rapidly absorbed, but not more so than a solution of glucose, and therefore possessed no advantage in that respect. Alcohol stimulated the taste endings in the mouth and caused the flow of saliva and the psychic secretion of gastric juice. There was a direct stimulus to the fundus of the stomach initiating a flow of juice; but concentrated solutions might inhibit secretion. Alcohol was excreted in milk. This occurred only after large amounts, and the maximum amount would be too small to affect sucklings. Its diuretic action was due to fluid intake; perhaps it might be due to something else, but despite a diligent search of the literature, no conclusive information could be obtained. Dr. Shaw went on to say that in the past there had been many misconceptions, both lay and professional, concerning the therapeutic action of alcohol. Nearly every view held by physicians in the past had proved to be erroneous. A philosopher might ask, "can we trust our senses?", whilst a scientist might well inquire, "can we trust clinical experience?". The belief in the stimulant action of alcohol on the central nervous system, the heart or respiration, and in its action as a warmth-producer, had been abandoned. Its chief uses were now as an antipyretic, as a mild hypnotic, and as a supplier of energy whose absorption was independent of digestve enzymes, and it was therefore used in fever when absorption of other foodstuffs was impaired. It should be given in small repeated doses rather than in large doses, to avoid intoxication. Alcohol was also used as a disinfectant. It should be noted that 70% strength was better than absolute alcohol in this respect. It might be applied to the skin, but should not be trusted for instruments.

PROFESSOR P. MACCALLUM, of the Department of Pathology, University of Melbourne, said that his was the relatively limited task of presenting an outline of what was known of tissue changes commonly held to result from the taking of alcohol, and of some of the guesses as to how they came about. The clinically observable features of alcoholic intoxication might be summarized as indicating depression and confusion of functions at all levels—social, mental, physical and metabolic. Scientific investigation left no doubt of the pharmacological and psychological profundity of the observation that "wine is a mocker". The medical virtues remaining to alcohol were almost confined to its efficacy in about 70% solution as a skin antiseptic, as a test reagent *in vitro*, as a vehicle for certain pharmaceutical preparations, and as a fixative for pathological specimens. It was generally agreed that, except for absinthe and adulterations, the effects of alcoholic beverages were due to ethyl alcohol. It was a product of vital activity, and in minute quantity was present in all tissues. An oxidase for alcohol had been demonstrated in the liver tissue. Alcohol had the property of mixing with water in all proportions, and was to some extent a fat solvent. These properties explained the ease of its penetration of membranes and the relative uniformity of its distribution in the tissues. The main determining factor in the differences of tissue distribution appeared to be the tissues' free water content. The readiness and completeness of alcohol's oxidation in the body to water and carbon dioxide, and the fact that the energy so produced could be used by the tissues, would appear to make it an ideal food; but the very fact of its ready distribution limited its usefulness, since storage reserves were impossible. Though alcohol competed with carbohydrates for oxygen, it lacked flexibility of response in the economy of the body machine. Therefore, even as an energy food it had a limited value. This use was further limited by the fact of its narcotic effect even in small concentrations. Its diffusion retarded the vital processes generally, particularly those of oxidation, probably by upsetting the enzyme system responsible for oxygen exchange. It was true that the cells could to some

extent become adjusted to an environment containing much greater concentrations of alcohol than normal. The subject as a whole reflected the developed cell tolerance by a retained efficiency and absence of overt toxic consequences that would not be possible in persons not accustomed to its use. Reduction in this concentration resulting from sudden withdrawal of alcohol might, in cases in which tolerance was at a high level, induce physical and mental distress, or even precipitate *delirium tremens*. In the case of the chronic alcoholic, the amount of alcohol required in the morning to restore a condition of fitness to face daily routine was some measure of the degree of addiction. The effects of alcohol on metabolism might be seen in storage of fat in connective tissue (a feature subject to much individual variation), in increase of neutral fat in fat deposits in the liver, in the appearance of fat in heart muscle and kidney parenchyma, in the subintimal deposition of fat in arteries in the common sites, and even occasionally in the appearance of fat in obvious excess in the circulating blood. Another effect on fat metabolism was shown by the disappearance of acetone bodies after administration of alcohol to diabetics in whose blood they had appeared. In the chronic alcoholic the alimentary tolerance for glucose was diminished, and sugar appeared in the urine in a high proportion of cases, after test doses which did not readily affect the normal individual. That alcohol acted as a major factor in the disturbance of protein metabolism was demonstrated by the relationship of alcohol intake to the incidence of gout. Its role in sparing protein was also easily demonstrated experimentally, by its protective effect on animals reduced to the necessity of metabolizing protein for energy purposes.

Referring to the pathology of alcohol, Professor MacCallum said that the effects of alcohol on the alimentary tract were of importance in a variety of ways. Alcohol was peculiar, in that approximately a quarter of the intake was absorbed in the stomach and the remainder in the upper part of the small intestine. Its effects in stimulation of appetite and the reflex production of secretion in the stomach were obscured by psychic conditioning and by the accessory substances that gave beverages their distinctive flavours. Alcohol, especially in concentration, damaged surface cells, and congestion and leucoplakia might result in the œsophagus. The effects of alcohol on the stomach varied with circumstances, rate of intake, concentration, amount and relation to food. Vomiting might occur. Gastric motility was at first increased, but later diminished by the action of the alcohol. The secretion induced was watery and poor in enzymes and acid. A condition of acute congestion commonly resulted. In alcoholics chronic gastritis with variable congestion and impairment of the integrity of the mucous surface was common. Submucous and even frank hæmorrhages might occur. Hæmorrhage from varices in the lower end of the œsophagus was, of course, a feature of cirrhosis of the liver. A similar chronic condition was produced in the mucosa of the upper part of the small intestine. The altered state of the digestive tract was reflected in loss of appetite, and, importantly from the point of view of general nutrition and the supply of accessory factors, it resulted in unsatisfactory intake of food, both from this cause and from impaired digestion. It was usually stated that the products of abnormal fermentation in the intestinal tract might be absorbed and possibly play a part in the resulting ill health. There was little specific evidence that this was so. Diarrhœa might be induced and hæmorrhoids occur. The condition of the stomach might be expected to affect adversely the provision of hæmatopoietic factors, and this effect, it had been suggested, accompanying damage to the liver might enhance. Alcoholic drinks disturbed the distribution of fluid in the body by dilating peripheral vessels and altering the permeability of the capillaries. Distribution and the elimination of fluid appeared to follow closely the pattern of water disposal—diversion into the tissues preceding an elimination which did not remain parallel with ingestion. At the same time, the distribution and elimination of salt were correspondingly disturbed, and cramps might result. Persistent patchy dilatation of vessels, altered texture and condition of skin structures (*acne rosacea*, rhinophyma), and a suffused congestion of the conjunctiva, contributed to the appearance of the victims of over-indulgence in alcohol, commonly described as dissipated. These congestive changes were not, of course, confined to the skin. They were characteristically seen in the abdominal viscera and in other organs. In both acute and chronic alcoholism, the clinically observed enlargement and tenderness of the liver corresponded to the finding *post mortem* of congestion, usually together with considerable fatty infiltration. There had been much discussion on the relationship of cirrhosis of the liver to the intake of alcohol, and there was one form of cirrhosis known as "alcoholic". The justification for this title was extremely doubtful, and the occurrence of cirrhosis was certainly not directly attributable to alcohol. It occurred commonly in abstainers, and was uncommon in Scotland, where the spirit drinking which it was alleged to follow should have made it noticeable. The liver was obviously affected by the intake of alcohol apart from cirrhosis, and some degree of jaundice commonly accompanied the liver congestion. About 90% of the alcohol in the body was disposed of in the liver, and it was in the liver that the highest percentage of the alcohol oxidase was found. In this connexion, the fact that the excised liver of cats whose pancreas had been removed did not oxidize alcohol, appeared to indicate some influence of insulin in the maintenance of alcoholic oxidase. Disturbance of liver function was more likely to be reflected in the amount of storage fat than in cirrhosis. Experimental work on animals in the production of cirrhosis left the supposed cooperative action with alcohol by toxins from the bowel still a rather insufficient and ill-defined hypothesis. More definite causes were known, and associations of cirrhosis with other conditions had of late years gained new significance. Thus the association of cirrhosis of the liver with changes in the basal nuclei in Wilson's disease (hepato-cerebral degeneration) and in Wernicke's encephalopathy (*encephalitis hæmorrhagica superior*) suggested on one hand the operation of hereditary factors, and on the other, hypovitaminosis or avitaminosis. In both conditions alcohol might play a part, but only in some cases. The occurrence in several members of the same family of cirrhosis of the liver, with and without lenticular changes, might indicate an hereditary tissue susceptibility.

Discussing avitaminosis, Professor MacCallum said that the association of alcohol with manifestations of hypovitaminosis or avitaminosis had obvious importance, and it was supposed that alcohol prevented or inhibited the intake of vitamins B_1, B_2 and perhaps A. Colour was lent to the hypothesis by the fact that vitamin B_1 was a coenzyme in the oxidation of carbohydrate and the production of pyruvic acid, participating in a group of enzyme actions which was also concerned with the oxidation of alcohol in the liver. Closely linked was the occurrence in chronic alcoholics of polyneuritis affecting both sensory and motor nerves. Congestion, swelling and fibrous overgrowth appeared in epineurium, perineurium and endoneurium. In the axis cylinders nodose swellings might be found, and in the myelin sheaths, Wallerian degeneration. Occasionally phagocytic activity and leucocytic infiltration were seen. Optic neuritis and degeneration of the retinal cells, characteristic of methyl alcohol poisoning, did not occur with ethyl alcohol, though there might be impairment of colour vision fields. Probably changes observed in the central nervous system were to be ascribed to the factors concerned with avitaminosis; in Wernicke's disease capillary dilatation and proliferation and thickening of the vascular walls occurred, particularly in the region of the *corpora mammilaria*, the thalamus and hypothalamus, and the walls of the third and fourth ventricles. These areas were concerned, not only with many vital functions, but with mental and emotional states. About these vessels were myelinization, fibrous and astrocytic proliferation and small hæmorrhages. The association of such changes with a confusional mental state, found in some alcoholics usually together with "alcoholic neuritis", and known as Korsakow's psychosis, appeared to come into line with the association of similar lesions with carcinoma of the stomach, with other gastric and gastro-intestinal conditions, and occasionally with macrocytic anæmia, on a common basis of defective vitamin supply, especially vitamin B_1. Observation of the occurrence of pellagra-like syndromes (dermatitis, mental change and gastro-intestinal symptoms) in patients subsisting for long periods mainly on alcohol, reinforced such suggestions. Professor MacCallum went on to say that, though they were variable in intensity and difficult or impossible to correlate precisely with clinical findings, certain conditions were fairly constant in chronic alcoholism; they were pigmentary and other retrogressive appearances in the ganglion cells, the cells of Betz and other cells, and demyelinization of tangential and radial fibres in the outer laminæ of the cortex. Fatty changes were common in the vessels, and in the meninges endothelial vascular changes were thought to be responsible for the occurrence of hæmorrhage from relatively slight trauma. Thickening or œdema of the pia, chronic pachymeningitis and adhesions of the dura to the skull were not uncommon. The appearances in the brain after death from acute poisoning were also variable; perhaps the commonest finding was meningeal congestion. The brain itself might be œdematous or congested, and occasionally small petechial hæmorrhages were present. There was no characteristic abnormality to be found microscopically. A "wet" brain

was a not uncommon finding in chronic alcoholism, particularly in cases in which attacks of *delirium tremens* had occurred.

Professor MacCallum then said that in the heart, general loading with adipose tissue was frequent to a degree that might itself embarrass cardiac action. Fatty change in heart muscle might occur, and brown atrophy was common. Atheroma in the coronaries and in the heart valves was frequently advanced. The amount of diffuse or patchy fibrosis in heart muscle varied. Thickening of the valve cusps was also fairly common. These changes were, of course, quite non-specific. The occurrence of hypertension and consequent cardiac hypertrophy was not characteristic of alcoholic excess. In deaths from alcoholic excess, failure of the heart was nevertheless commonly blamed, and as a rule at autopsy the heart muscle was found to be flabby, and the right side of the heart was dilated and distended with dark fluid blood. Considerations of a similar kind applied to the occurrence of nephritis, which was affected in at least two ways by alcohol; fatty accumulation was common in the tubules and sclerotic changes occurred in the arteries. Essentially the development of nephritis was from other causes, and although alcohol might play a part in aggravating or accelerating its progress, it had no known specific relationship to any of the forms of nephritis, unless the arterial and nephro-sclerotic changes that were so common in gouty subjects were included as perhaps they should be. The lungs (including bronchi, trachea and larynx) were commonly congested, and occasionally the lungs were noticeably œdematous. The insensitivity of the mucous membrane during unconsciousness endangered the patient if vomiting occurred. Alcohol inhibited the ciliary action of bronchial epithelium—notable evidence of a direct effect on cells. Chronic alcoholics fairly frequently died of pneumonia, and another general effect of alcohol on cellular function was seen in failure of leucocytosis. This was usually regarded as significant in determination of the result, and was eloquent also of the depression of hæmatopoietic activity in the bone marrow. A further effect of alcohol on the leucocytes was interference with their enzyme oxidase. Such observations provided some justification for the general statement that alcoholics had a lowered resistance.

Professor MacCallum went on to say that alcohol did not reach concentrations in the tissue which would render it unsuitable for bacterial growth. Indeed, the concentration was such that the tissue might well provide nutriment for certain bacteria. There was no reason to suppose that alcohol had any virtues in the prevention of infection. Its action in the body was rather to enhance the damaging effect of poisons and toxins, both directly and indirectly, through induced hypovitaminosis, and generally to interfere with healing processes and restitution. Alcohol had been found to facilitate the absorption and to increase the action of other substances, such as carbon tetrachloride, potassium iodide and arsenic, and hence also their pathological effects. Alcohol was a habit-producing drug, but not powerfully so; the addiction itself might be a symptom of nervous system defect. It would be futile to include the varied pathology of such conditions in the pathological manifestations of alcoholism, greatly though alcohol might aggravate the basic defect. The repute of alcohol as an aphrodisiac rested rather on the removal of social inhibitions than on a physiological basis. Indeed, so far as the effects of alcohol were concerned, desire was apt to outrun performance. It was scarcely necessary in the present company to mention the influence of the depression of cortical controls on the incidence of sexual laxity and venereal disease. The possible effect of alcohol on offspring had been the subject of investigation, and so far as careful experiments on guinea-pigs went, there was no evidence whatever that alcohol injured the germ cells or that any hereditary abnormality resulted from its presence. Fertility was unaffected in males or females. "Alcoholic" parentage did not appear to have any directly adverse effect on intrauterine or extrauterine development. The great individual variation in the psychic and physiological responses to alcohol argued for the importance of constitutional differences in their determination, and this was supported by the hereditary character of some of the diseases developed—gout, Wilson's disease, glycosuria. Alcohol revealed the inherent defect, or produced a disease result, either alone or in combination with other factors—factors which, without alcohol, were in other circumstances capable of producing a part or the whole of a characteristic syndrome. There was, therefore, nothing specific about the morbid anatomy of alcoholic poisoning. Professor MacCallum thought that this was inherent in the properties which caused its general diffusion, and in the generality of the vital process of oxidation, with which essentially it interfered. It was not specifically local in its effects, but it would join forces with, and wear the uniform of, any other noxious agent in an insidious assault on the bodily estate.

Professor MacCallum then discussed vital statistics. He said that comparison of ages and causes of death among alcoholics with those among the general population in America showed that deaths from causes in which alcohol was a probable factor occurred at an earlier age than deaths from all causes. Persons with access to alcohol were notoriously "bad lives". Comparisons of the systems listed as concerned in causing death showed that liver, kidneys and heart (in that order) were much more frequently recorded among alcoholics than among the general population. The lungs and the central nervous system, and general debility, were slightly more prominent in the alcoholic list, but bronchitis, tuberculosis and senility were commoner in the general population than in alcoholics. It was of interest to note that these statistics provided no support for the popular belief that alcohol predisposed the subject to phthisis.

In view of all that had been said about the deleterious effects of alcohol, it was of interest perhaps to know what effect it had on the duration of life. The most extensive and critical investigation of this kind that had been carried out was by Raymond Pearl, who examined the statistics of a socially and economically homogeneous group of approximately 154,000 working-class white people in Baltimore. The men and women were classified separately as abstainers (men 21,000, women 41,000), moderate drinkers (men 42,000, women 21,000) and heavy drinkers (men 26,000, women 2,000), with divisions of the drinkers into subgroups (according to habit) of "quantity unspecified", "occasional" and "steady". Comparison was made of their statistics with those of the United States Life Tables for whites of the same ages. Pearl's figures gave the following information: (i) That at every age from thirty to one hundred years the "all-moderate" group, independently of sex, had a slightly higher expectation of life than abstainers of the same age. (ii) (*a*) That in the "all-heavy" group, males had a much lower expectation of life (at all ages) from thirty to one hundred years than the male "all-moderate group" (42,000). (*b*) That the "all-heavy" group (males, 26,000) had a much lower expectation of life between thirty and sixty years than the male abstainer (21,000) group, but between sixty and one hundred years had a slightly higher expectation of life than the corresponding abstainers. This was regarded as possibly due to the selective result of higher death rates before sixty years. (*c*) That the female "all-heavy" group had a much lower expectation of life from thirty to one hundred years than the female abstainer or "all-moderate" groups. (*d*) That of the females, the "moderate steady" group had the consistently highest expectation of life from thirty to one hundred years. (*e*) That of the males, the "moderate steady" group had the consistently highest expectation from thirty to seventy years, but from seventy to one hundred years the "all-moderate" group had a slightly higher expectation. Pearl's study confirmed the opinion that heavy drinking was very deleterious. It also supported the findings of the Medical Research Council's Alcoholic Investigation Committee that it did not follow that consistent moderate use of alcohol shortened life. The committee was unable to prove that moderate use of alcohol had any effect at all one way or the other on longevity. Pearl's figures slightly favoured the moderate use of alcohol. The two life curves were not widely different; but what advantage there was lay with the moderate drinkers. There was, however, difficulty in defining what was "moderate use", and Pearl included in the "heavy" group regular drinking of alcohol at meals—a pint or two of beer, a bottle of claret or a few glasses of whisky and soda per day. Length of life, however, was not the only socially or personally important consideration. The consumption of alcohol in quite small amounts induced temporarily in the subject a complacent acceptance in himself, as best, of what could be only a second best, and such a practice had to be condemned as a derogation of human dignity. Socially, the delights of euphoric illusion had to be set against the sum of social inefficiency, disease, misery and degradation.

Professor BacCallum said that, as a pathologist, he could say nothing good of the consumption of alcohol. He was not a teetotaller; but he would be less than honest if medically or scientifically he lent any support to advocacy of the use of alcohol, or failed to expose it for the fraud he knew it to be. He had never known anyone to suffer by not taking alcohol. He had known—all those present had known—many to suffer through drink. Professor MacCallum concluded by quoting the physiologist Starling, who went so far as to edit a book in favour of the use of alcoholic drinks. But as a responsible scientist writing for students of medicine, his commendation was confined to taste and smell, and he ended thus:

If taken in any quantity at one time, it causes a temporary abolition of those processes of inhibition and control which have been the determining factors in the survival of the race throughout the struggle for existence.

DR. JOHN K. ADEY, Medical Superintendent of the Royal Park Mental Hospital, said that the administration of the same quantity of alcohol had different effects on different people, some being able to absorb large amounts with impunity, others showing mental and physical changes as soon as they commenced to drink. Each person had his own threshold of alcoholism—the maximum amount of alcohol that he could absorb in a given time without showing marked effects. Dr. Adey said that he had little faith in the laboratory experiments on the effects of administering varying quantities of alcohol and then making the recipient add up numbers or perform manual tests. Alcohol given in the cold scientific atmosphere of the psychological laboratory had a totally different effect from that of an equal quantity taken in congenial social surroundings at a convivial party. Experience showed that the amount of alcohol that could be absorbed with impunity in a given time decreased under the following conditions: (i) With increasing age. Many patients were admitted into the Receiving House at about the age of forty years. They all informed Dr. Adey that they used to be able to take alcoholic drinks, but now they could not "hold their beer". (ii) After head injury. Any severe traumatism to the head necessitating a stay in hospital of several weeks appeared to make a man more susceptible to the effects of alcohol. (iii) In epilepsy. Epileptics should be teetotallers for the whole of their lives. (iv) After continued alcoholic excess. Continued excessive intake of alcohol over a period of years led to a gradual mental deterioration, even if there was little sign of excess at any particular period. Alcoholism was a complicating factor in many mental diseases, and it was a general rule that if a man who has been uniformly sober for most of his life began to drink heavily, there was probably some acute underlying cause. Manic patients felt so extraordinarily cheerful that they were willing to drink with anybody and everybody. A melancholic would frequently prescribe for himself the only medicine he knew, and would drink to drown his sorrows, with the result that the subsequent reaction increased his melancholia. Many of the psychoneuroses were obscured by alcoholism, particularly anxiety neurosis, as the patient felt that alcohol helped to tide him over his difficulties. Dipsomania was a disease in which a man had long intervals—perhaps six to twelve months—of total abstinence or sobriety, and then had a bout of heavy drinking, usually lasting until his money ran out or he suffered from *delirium tremens*. That this was a physical disease was shown by the fact that if his friends took him to a mental hospital as soon as they saw the premonitory symptoms of an alcoholic outburst, so that there he was prevented from access to alcohol, the non-existent drinking bout was replaced by an attack of confusional insanity from which the patient recovered after the usual course of sedatives and sleeping draughts.

DR. GUY SPRINGTHORPE said that he had been asked to discuss the question of alcohol—and by that presumably was meant the consumption of alcohol—in relation to sociology. Dr. Springthorpe had no particular knowledge of herds and races, but perhaps some glimmerings of insight into the vagaries of human personality, on which social behaviour was based. He proposed to make a few remarks on alcoholic beverages as they concerned different individuals—not physiologically, but psychologically. There was a suspicion in his mind that some listeners anticipated that his appearance on the platform that evening was somewhat in the role of devil's advocate. However, in advocating the sensible use of alcohol by such as wished to take it, he hoped to give the demon of drink his due.

Dr. Springthorpe said that one of the weaknesses of medical science had been the assumption that all human beings were more or less the same. Particularly had this been the case when disease was being considered. As his father used to put it, doctors said that "Brown's got pneumonia", whereas it should be "pneumonia's got Brown". The truth was that everyone was different from everyone else, and the range of variation was enormous. These individual differences were particularly important in the field of psychological medicine. It was, moreover, difficult, and at times impossible, to demarcate the limits of normality from the beginnings of abnormality. Who was it had said that "all madmen are a little sane, and all sane men a little mad"? In considering the question of alcohol drinking from that viewpoint, Dr. Springthorpe said that he proposed deliberately to oversimplify and distort, *à la* Dobell (but less artistically), by subdividing humanity into three groups. The first was the largest, containing in his opinion about 80% of the population. These were the reasonably stable persons—not perfect characters, of course—who were not too unhappy or maladjusted; who in spite of their peculiarities and foibles could usually gamble without losing a fortune, get into an argument without a fight, eat a dinner without being sick, take a holiday in mixed company without indulging in sexual orgies, and drink in moderation. And why did some of these people take alcohol? The answer was simple—because it made them feel happier and more at ease. A number of lesser reasons had been given, and one might quote authorities from Saint Paul to G. K. Chesterton. That was the majority. There was a minority, however, who did not stand up to their troubles and disappointments quite so well; who for reasons of constitution or maleducation tended (unconsciously) to run away from difficulties. All human beings were escapists some of the time; these people were escapists most of the time. In psychological parlance they formed the pre-neurotic section of the community. Some of them in the end would drink to excess; a few would become drunkards. Whilst drunkenness often led to deplorable results, in fairness to both sides, it should be mentioned that not all who drank to excess were bad characters. Crimes and other social misdemeanours might be committed by persons "under the influence"; but a great many more nasty actions were perpetrated by the stone-cold sober.

Dr. Springthorpe went on to say that there were two ways of helping the pre-neurotic personality in relation to alcohol. The first, and best, was by tackling the personality defect, when possible by preventive methods—by education. By education he meant proper education for full development and complete living. When this failed, psychiatric treatment was required. The second approach was from the alcohol angle, by improving drinking amenities. It was important to remember that, human nature being what it was, unstable types would never be eliminated, just as by studying comparative sociology it was reasonable to conclude that there would always be alcohol consumption, whether the race was savage or civilized.

Dr. Springthorpe then referred to the third—and smallest—subdivision. It consisted of those who, by reason of inherited psychopathy or of frustration in childhood, became warped and suspicious adults—those who, unable to enter fully into the emotional satisfactions of life, derived pleasure by preventing others from so doing. Owing to the irrational nature of their peculiarity, they had little or no insight into their mental processes. Their ideas, being emotionally conditioned, were seldom amenable to argument. These people might be termed the pre-psychopaths of the community. In some instances their crankiness took the form of extreme wowserism, and not a few of the more fanatical prohibitionists were of this category. By their very intemperance they played into the hands of opponents of practical reform. Unfortunately the pre-psychopaths, like the pre-neurotics, would always be in the community, and they were the least amenable to treatment.

This, then, was the picture—purposely over-simplified. To improve things, by all means let liquor reform be advocated—it was long overdue. At the same time, Dr. Springthorpe would like to see a league to prohibit prohibitionists. But too much should not be expected. What was practicable was to agitate for improved facilities for the sensible drinker, free from the prying eye of the busy-body and the bureaucrat. This led him to his sole contribution to sociology—an account of recent happenings at Invercargill. For nearly forty years, this town in southern New Zealand, owing to that ridiculous procedure known as local option, had been legally "dry". Actually—so his informant, who lived there for ten years, had told him—the worst kinds of drinking were rife. At the last election, by the intelligent use of the soldiers' vote, the necessary two-thirds' majority was obtained and the long drought was broken. The question then arose, should they revert to the old-time "pub" or try something better? After consideration—and one could imagine the pressure politics that went on—it was decided that a municipal licensing commission should be appointed by the Government. This was a body of four, the president being a draper and the others including a farmer, a business man and so on. They were in complete control, subject only to the licensing laws of New Zealand regarding drinking hours. These were similar to the Victorian laws and included 6 o'clock closing. This was what had happened. The commission appointed a general manager—an expert with long experience in the liquor trade—and had brought in the following innovations. Firstly, no "vertical" drinking; to do this they had bought the old public houses, intended to pull out the bars, fix up café-like accommodation, and put

in their own staff. In addition, the largest tea-house in the town had been purchased and others had been rented. In all these places both alcoholic and non-alcoholic drinks could be obtained. That was to say, in a tea-room mother could have a glass of beer, father a cup of tea and Willie an ice cream soda, without anyone raising their eyebrows or haling them before a magistrate. This novel experiment in common sense might break down. The public would need educating, and extremists, both "dry" and "wet", would do all they could to make it fail. Dr. Springthorpe sincerely hoped that the commission would have the wisdom and perseverance to make it succeed. He said that he would make no attempt to describe the anomalies and absurdities of the various licensing laws in the Australian States. In Victoria many of them had recently been ventilated before a royal commission. Little had been done, and the situation cried aloud for some reform along the lines of Invercargill's. How long must they oscillate between the two extremes of "pubs" and prohibition, when, if they wanted to, they could enjoy the happy medium of sensible drinking? But those present would say that a country got the "pubs" and prohibitionists—and the politicians—it deserved; Dr. Springthorpe was inclined to agree with them.

DR. JOHN DALE expressed appreciation of the value of the contributions of the opening speakers and invited a general discussion.

DR. H. F. MAUDSLEY, speaking as a physician who was frequently consulted on clinical problems associated with the unwise use of alcohol, drew attention to the need of more certain legal machinery for the prevention of the wrecking of the homes of those persons in whom alcoholism was already established. After spending money on alcohol for years a man might became more and more difficult for his family or even be frankly paranoiac. Dr. Maudsley asked Dr. Adey whether there was any possibility of securing an amendment to the *Inebriate Act* to ensure legal certification and subsequent compulsory commission to an institution of the person so certified. All that could be done at present was to obtain his admission to a public receiving house for approximately a week; then when the patient became sober he was no longer deemed insane and was discharged. Dr. Maudsley went on to say that there were only one or two private hospitals for female patients and none of which he knew for male patients suffering from inebriety of psychiatric importance. At these private hospitals the matrons were unable to accept responsibility beyond ordinary hospital responsibility for the safe custody of the patient. If an inmate escaped from the hospital and had access to alcohol before being returned, the matrons were inclined to refuse readmission of the patient. Dr. Maudsley observed that alcoholism might obscure such mental diseases as general paralysis of the insane or a psychosis; but in other instances the malady was genuinely and simply alcoholism. The problem in practice was a trying one, and he wished to know what could and should be done about it.

Dr. J. K. Adey, in reply to Dr. Maudsley, agreed that something should be done legislatively for the restraint of chronic alcoholic patients who were not otherwise insane. When such a patient became sober and there was no residual evidence of insanity, a medical superintendent of a mental hospital had to allow the patient to leave the institution. The dictum had been laid down that it was not the safety of wives but the sanity of patients that had to be considered in reaching a decision to hold a patient or to let him go. The legislation that Dr. Adey would wish to support was certification as a chronic inebriate, with the provision that such a person so certified should be committed for a specified length of time to a suitable institution. The period should not be less than six months and could with advantage be so long as two or even three years.

DR. R. R. WETTENHALL said that the subject had been presented well from various scientific aspects. He added that dermatological inflammation needed rest for its cure: it was desirable to keep the temperature of the skin even and cool. As alcohol aggravated inflammation in the skin, producing flushing and hypertrophy of the glandular tissues and increasing perspiration, the intake of alcohol should be interdicted. He went on to suggest that pellagra-like lesions in irregular positions might be ascribed to habitual use of a stimulus such as alcohol. Dr. Wettenhall also took the opportunity to stress the importance for the general public of the discussion on the effects of the consumption of alcohol. He related an incident of the last war, in which unsatisfactory results could be attributed to excessive consumption by young officers, who even took alcoholic beverages in winter time with the snow lying on the ground. Dr. Wettenhall was an advocate of temperance, but on account of the damage done in later life, he deplored the frequency with which young fellows started out on alcoholic careers at the tender ages at which many of them joined the army. He considered that it was of great public importance to decide what should be done to prevent excessive consumption of alcohol by those serving in the forces.

DR. C. H. DIXON asked Dr. Adey whether he could say what proportion of non-psychotic chronic alcoholics were curable.

Dr. J. K. Adey replied that the prognosis was extremely bad when the condition had gone on for so long as five years.

Dr. H. F. Maudsley said that men of character could be cured if the physician could secure the cooperation of the patient.

Dr. Dale, from the chair, expressed appreciation of the quality of the symposium. He considered that there was a great deal to be said for liquor reform. There was a group of doctors in Queensland actively circularizing their colleagues to join in concerted action to bring about the desired reforms. Dr. Dale was not surprised that with the succession of a Great War, a great depression and another war many people felt that escapism was indicated. Perhaps the most influential reform would be for all to have a better way of life. If the standard of living was raised and happiness was the rule rather than the exception, the need for escapism would be minimal and chronic alcoholism as an addiction would be rare.

Professor P. MacCallum spoke again, to stress the point that the public had no means of getting reliable information about alcohol. From the scientific point of view one should not form judgements passed on the statements of those who had imbibed the alcohol. The medical profession had a great responsibility to the public, and individual members must not be influenced by their own pleasure. It was a proper subject concerning which the medical profession should show a definite quality of leadership.

NOTICE.

THE General Secretary of the Federal Council of the British Medical Association in Australia has announced that the following medical practitioner has been released from full-time duty with His Majesty's Forces and has resumed civil practice as from the date mentioned:

Dr. Herbert Earnshaw, 113, Wickham Terrace, Brisbane (August 27, 1945).

The Royal Australasian College of Physicians.

MEETING AT SYDNEY.

AN ordinary meeting of the Royal Australasian College of Physicians will be held at Sydney on Thursday and Friday, September 27 and 28, 1945. The programme will be as follows:

Thursday, September 27, 1945.

10.15 a.m.—Council meeting in the Council Room of the College. The admission of new members will take place at this meeting.

2.15 p.m.—Meeting of the general body of Fellows in the Stawell Hall of the College.

2.30 p.m.—First scientific session in the Stawell Hall of the College. "Dissecting Aneurysm of the Aorta", Dr. J. H. Halliday and Dr. J. S. Robertson. "Marrow Biopsy in Hæmatological Diagnosis", Dr. A. J. Canny. "Discussion of Pulmonary Interstitial Emphysema with Pneumomediastinum, Subcutaneous Emphysema and Pneumothorax, with Case to Illustrate", Major J. F. C. C. Cobley. Afternoon tea will be served at 3.45 p.m. and the presentation portrait of Sir Sidney Sewell will be unveiled by the President at 4 p.m.

Friday, September 28, 1945.

10.15 a.m.—Continuation of Council meeting in the Council Room of the College.

2.15 p.m.—Second scientific session in the Stawell Hall. "Simmonds's Disease", Dr. Lorimer Dods. "Psychotic States in Soldiers", Lieutenant-Colonel A. J. M. Sinclair. "Hyperidrosis", Professor C. G. Lambie and Dr. Alice J. Palmer. "Penicillin in Bronchiectasis", Dr. H. Maynard Rennie.

8.15 p.m.—Address by Professor Dixon Wecter, "Literature and the Clinical Point of View", in the Stawell Hall of the College. The wives of Fellows and members are invited to attend. Supper will be served at the conclusion of the address.

The Royal College of Obstetricians and Gynaecologists.

MEMBERSHIP EXAMINATION IN AUSTRALIA.

THE Royal College of Obstetricians and Gynæcologists has agreed to hold an examination in Australia for Membership (M.R.C.O.G.) if in the opinion of the Reference Committee a sufficient number of candidates present themselves.

Applicants must have been three years on the Register and have held (*a*) a six months' resident appointment in the medical or surgical department of a general hospital, (*b*) a six months' resident appointment at an obstetric hospital, (*c*) a six months' resident appointment in a gynæcological hospital or department of a general hospital; (*b*) and (*c*) may be combined in one appointment, but must extend for a period of not less than one year. Records of 25 selected obstetrical cases and 10 gynæcological cases must be submitted together with a 2,000-word commentary in each subject. The examination consists of two written papers on the anatomy, physiology and pathology of the female reproductive organs, obstetrics and gynæcology with clinical and *viva voce* tests.

It is assumed that the examination will not be held until service candidates, who have not already complied with the regulations, have had an opportunity to do so.

Applications and any inquiries should be sent to Professor Marshall Allan, University of Melbourne.

Correspondence.

THE PHARMACEUTICAL BENEFITS ACT, 1944.

SIR: I can assure Dr. Jury that I for one do not consider him a "hero" for writing a letter to the *West Australian* bitterly slating the British Medical Association. I have never heard of a trade unionist doing that to his union, and surely we can boast of equal *esprit de corps* as industrialists.

It reminds me of the man in Hyde Park, London, who was trampling on a Union Jack before a crowd. A policeman was asked why he did not arrest him. "Well", he replied, "he is trampling on his own flag."

Yours, etc.,

F. W. SIMPSON.

271, Cambridge Street,
Wembley Park,
Western Australia.
August 28, 1945.

THE PREVENTION OF FRACTURES DURING SHOCK THERAPY.

SIR: Dr. Hamilton (August 25, 1945) invites comment on his suggested techniques for lessening the incidence of fractures in convulsive therapy. Briefly I find his suggestions unacceptable, for there is already in use a simple and effective technique which minimizes fractures and which has the merit of sparing depressed and apprehensive patients the mental discomfort of the proposed restriction by plaster jacket, spinal brace, or "modified strait-jacket".

This technique, which I have employed in well over a thousand convulsions, consists in placing a small firm pillow under the lumbar and lower thoracic spine, between patient and mattress, and training three nurses to hold the patient during the convulsion as follows. One with a hand on each of the patient's thighs to oppose raising of the knees during the initial flexor spasm (and thereby prevent forward flexion of the spine) and one on either side of the patient's trunk, each with one hand on a shoulder to prevent it rising from the bed, and the other holding a wrist, so that the patient's arm is adducted at the shoulder and flexed at the elbow. A fourth nurse, of course, adjusts the electrodes, inserts the mouth gag and controls the jaw. Sometimes, owing to retrograde amnesia, a patient will not remember the preliminary taking up of positions; and when he does, there is nothing very alarming to recall about the routine.

When only two limb-controlling nurses are available, each can stand on one foot and use the other knee to control the patient's thigh nearer to her, while controlling an arm with her hands.

Experienced nurses can control and vary the pressure used during the convulsion in a manner whch could not be obtained with restraining devices.

Yours, etc.,

R. EUAN MACLEAN.

Mental Hospital,
Mont Park,
Victoria.
August 27, 1945.

INTERVERTEBRAL DISK DISEASE: NEW SYNDROMES AND NEW CONCEPTS.

SIR: One cannot read Dr. Young's paper of August 25 without being arrested by his enthusiasm for the intervertebral disk pathology and by the ingenuity of some of his hypotheses. It has, however, been wisely stated that the value of hypothesis lies not so much in the ingenuity of invention as in the labour of verification. It is to be regretted that the former certainly outweighs the latter in Dr. Young's paper. Dr. Young at times lends to his statements such an *"ex cathedra"* quality that one may almost forget that they are still hypotheses. For instance:

"These flexion and lateral flexion deformities are not primarily due to muscular spasm, as is so often stated, for they may persist under anæsthesia, and further, there is no muscle which will produce the localized deformities that sometimes occur. These deformities are due to the protrusion of a piece of disk which prevents the vertebræ from being extended or flexed to the affected side."

I, for one, challenge the statement that these deformities mentioned do not disappear under adequate anæsthesia, and I would indeed be reluctant to dismiss the almost incomprehensibly complex back musculature as being incapable of producing such localized deformity. Even if the deformity be net due to muscle spasm, I am quite sure, from an experience of operating on a large series of cases, that the damaged disk is quite incapable of primarily causing deformity. It is not, as shown in Dr. Young's drawings, a neat little ball which may roll about in globular integrity in response to the surgeon's manipulations, but it is a little mass of soft structureless material with the resistance and consistence of wet blotting paper. If the site of the damaged disk has any effect on intervertebral alignment, it would be in the nature of a subsidence and not a separation of the vertebræ.

The surgeon who wishes to restrain the surgical enthusiasm of a physician plays an unusual role, but some experience with the beneficial effects of rest obtained by proper immobilization in many cases of low back pain and in some undoubted disk syndromes, would lead me to regard the early and radical surgery advocated as being unnecessary, and possibly harmful. No one can doubt the good effects of conservative surgery on the intractable sciatica due to mechanical pressure from a disk fragment or protrusion, where localization can be accurate and operation not destructive. One may well doubt the benefits accruing from operation on low back pain where localization cannot be accurate and operation is destructive.

In his discussion of cervical disk syndromes, a case of third disk displacement is quoted. The signs are said to provide a fascinating example of applied anatomy. To any surgeon who has repeatedly cut the nerve of supply to the infrahyoid muscles without achieving the effect of the tongue rising in the mouth from unopposed action of the mylohyoid, this hypothesis is indeed fantastic. In any case the hyoid is much more firmly fixed by ligaments than by muscles and won't rise into the mouth.

Are we to assume that anyone with a pain in the neck who thinks he has a swelling of the tongue—a fact quite incapable of demonstration—is to be labelled a third cervical disk syndrome?

There is no doubt, and this is a great advance, that most cases of a certain type of sciatica and some cases of brachial neuralgia are due to intervertebral disk pathology. We would do well, however, to avoid the dangers inherent in trying to reduce all pains and disabilities of the back, neck and limbs to the common denominator of one pathological lesion. If we fall into this habit it could appear that the orthodox view of chiropraxis may be a little harsh.

Yours, etc.,

DOUGLAS MILLER.

Craignish,
185, Macquarie Street,
Sydney.
August 31, 1945.

Post-Graduate Work.

DEMONSTRATIONS ON CLINICAL PATHOLOGY AT MELBOURNE.

THE Melbourne Permanent Post-Graduate Committee announces that Dr. Hilda Gardner will give a series of four lecture demonstrations on clinical pathology in the Pathological Laboratory, Royal Melbourne Hospital, on Tuesdays, at 5 o'clock p.m.: October 2, allergic conditions; October 9, bacteriology; October 16 and 23, hæmatology.

The fee for this course is £2 2s., and entries should be in the hands of the Secretary, Post-Graduate Committee, College of Surgeons Building, Spring Street, C.1, by September 20. Medical officers who have been on full-time active service during the war are exempt from these fees.

Obituary.

MICHAEL JAMES O'SHEA.

WE regret to announce the death of Dr. Michael James O'Shea, which occurred on September 6, 1945, at Burwood, New South Wales.

Corrigendum.

A LETTER has been received from the Secretaries to the Trustees of the Queensland Medical War Benefit Fund, 1943, stating that the name of Dr. J. G. Avery was omitted from the list of contributors in the report sent to this journal and published in the issue of August 25, 1945.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Harrison-Potter, Frances Del, M.B., B.S., 1945 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Cuthbert, Antony Bevan, M.B., B.S., 1945 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Wilkinson, Richard, M.B., B.S., 1943 (Univ. Sydney), (Captain), Merrivale Street, Tumut.

Berger, Pinkas, M.D., 1935 (Univ. Bratislava), registered in accordance with the provisions of Section 17A of the *Medical Practitioners Act*, 1938-39, NX77177 Captain P. Berger, 17, Douglas Parade, Rose Bay.

Roberts, Arthur Edward, provisional registration, 1945, Melbourne Road, East Lindfield.

Terrey, George Russell, M.B., B.S., 1944 (Univ. Sydney), 38, Stanton Road, Mosman.

Medical Appointments.

Dr. A. M. Jones has been appointed Government Medical Officer at Cracow, Queensland.

Diary for the Month.

SEPT. 17.—Victorian Branch, B.M.A.: Hospital Subcommittee.
SEPT. 17.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.
SEPT. 18.—Victorian Branch, B.M.A.: Organization Subcommittee.
SEPT. 18.—New South Wales Branch, B.M.A.: Medical Politics Committee.
SEPT. 19.—Western Australian Branch, B.M.A.: General Meeting.
SEPT. 20.—South Australian Branch, B.M.A.: Council Meeting.
SEPT. 20.—Victorian Branch, B.M.A.: Executive Meeting.
SEPT. 20.—New South Wales Branch, B.M.A.: Clinical Meeting.
SEPT. 25.—New South Wales Branch, B.M.A.: Ethics Committee.
SEPT. 26.—Victorian Branch, B.M.A.: Council Meeting.
SEPT. 27.—New South Wales Branch, B.M.A.: Branch Meeting.
SEPT. 28.—New South Wales Branch, B.M.A.: Annual Meeting of Delegates.
SEPT. 28.—Queensland Branch, B.M.A.: Council Meeting.
OCT. 2.—New South Wales Branch, B.M.A.: Council Quarterly Meeting.
OCT. 3.—Victorian Branch, B.M.A.: Branch Meeting.
OCT. 3.—Western Australian Branch, B.M.A.: Council Meeting.
OCT. 4.—South Australian Branch, B.M.A.: Council Meeting.
OCT. 5.—Queensland Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract practice appointments in Western Australia. All Public Health Department appointments.

Editorial Notices.

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All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such a notification is received within one month.

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